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(54) Title: NOVEL HCV NON-STRUCTURAL POLYPEPTIDE

(57) Abstract: Polypeptides comprising a mutant non-structural Hepatitis C virus useful in diagnostic and/or immunogenic compositions are disclosed, in which the mutant is an N-terminal mutation that functionally disrupt the catalytic domain of NS3. Polynucleotides encoding these polypeptides, host cells transformed with polynucleotides and methods of using the polypeptides and polynucleotides are also disclosed.



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5 **NOVEL HCV NON-STRUCTURAL POLYPEPTIDE**

FIELD OF THE INVENTION

10 The present invention relates to polypeptides comprising a mutant non-structural Hepatitis C virus ("HCV") polypeptide useful for immunogenic compounds for use against HCV, methods of preparing and using the same, and immunogenic compositions comprising the same. The present invention also relates to compositions comprising (a) a mutant non-structural HCV polypeptide and (b) a viral polypeptide that is not a non-structural HCV polypeptide and methods of using these compositions.

15

BACKGROUND OF THE INVENTION

HCV is now recognized as the major agent of chronic hepatitis and liver disease worldwide. It is estimated that HCV infects about 400 million people worldwide, corresponding to more than 3% of the world population.

20 Hepatitis C virus ("HCV") is a small enveloped RNA *flavivirus*, which contains a positive-stranded RNA genome of about 10 kilobases. The genome has a single uninterrupted ORF that encodes a protein of 3010-3011 amino acids. The structural proteins of HCV include a core protein (C), which is highly immunogenic, as well as two envelope proteins (E1 and E2), which likely form a heterodimer *in vivo*, and non-structural proteins NS2-NS5. It is known that the NS3 region of the virus is important for post-translational processing of the polyprotein into individual proteins, and the NS5 region encodes an RNA-dependant RNA polymerase.

25 Virus-specific T lymphocytes, along with neutralizing antibodies, are the mainstay of the antiviral immune defense in established viral infections. Whereas CD8⁺ cytotoxic T cells eliminate virus-infected-cells, CD4⁺ T helper cells are essential for the efficient regulation of the antiviral immune response. CD4⁺ T helper cells recognize specific antigens as peptides bound to autologous HLA class II molecules (viral antigens or particles are taken up by professional antigen-presenting cells, processed to peptides, bound to HLA class II molecules in the lysosomal compartment,

and transported back to the cell surface). Several observations support an important role of CD4⁺ T cells in the elimination of HCV infection. Tsai *et al.*, 1997 Hepatology 25:449-458; Diepolder et al 1995 Lancet 346: 1—6-1009; Missale et al 1996 JCI 98: 706-714; Botarelli et al 1993; Gastro 104: 580-587; Diepolder et al 1997 J.Virol 71:

5 6011. Immunogenic peptides usually have a minimal length of 8-11 amino acids. However, since the peptide binding groove of HLA class II molecules seems to be open at both ends, longer peptides are tolerated. Thus peptides eluted from HLA class II molecules are typically in the range of 15-25 amino acids. HLA class II molecules are extremely polymorphic and each allele seems to have its individual requirements for
10 peptide binding. Thus the HLA class II repertoire of a given individual determines which viral peptides can be presented to T cells. Recognition of the specific HLA-peptide complex by the T cell receptor accompanied by appropriate costimulatory signals lead to T cell activation, secretion of cytokines, and T cell proliferation.

Numerous studies demonstrate that HLA Class II restricted CD4⁺ responses are
15 determined by stimulating peripheral blood mononuclear cells with recombinant viral antigens or peptides. Botarelli *et al.*, (1993) Gastroenterology 104:580-587; Farrari *et al.*, (1994) Hepatology 19:286-295; Minutello *et al.*, (1993) C. J. Exp. Med. 178:17-25; Hoffmann *et al.*, (1995) Hepatology 21:632-638; Iwata *et al.*, (1995) Hepatology 22:1057-1064; and Tsai.*et al.*, (1995) Hepatology 21:908-912.

20 Polyclonal multispecific CD8⁺ T cell responses have been detected in patients with chronic hepatitis C. Additionally, CD8⁺ CTL's were shown to be important in resolving acute HCV infection in chimpanzees (Cooper *et al.*, Immunity 1999). About 50% of patients with chronic hepatitis C demonstrate a detectable virus-specific CD4⁺ T cell response, which is most frequently directed against HCV core and/or NS4 and
25 tends to be more common in patients who achieve sustained viral clearance during interferon- α therapy.

Depending on the pattern of lymphokines, CD4⁺ T helper cells have been classified as TH1, TH0, or TH2. Cytokines of the TH1 type are typically IFN- γ , lymphotoxin, and interleukin-2 (IL-2), which are believed to support activation of
30 virus-specific CD8⁺ T cells and natural killer cells. The TH2 cytokines IL-4, IL-5, IL-10, and IL-13 are important for B cell activation and differentiation, thus inducing a humoral immune response.

During acute hepatitis C infection a strong and sustained TH1/TH0 response to NS3 and possibly to other nonstructural proteins is associated with a self-limited course of the disease. Diapolder *et al.*, (1995) Lancet 346:1006-1007, showed all CD4⁺ T cell clones to have a TH1 or TH0 cytokine profile, suggesting that the clones support
5 cytotoxic immune mechanisms *in vivo*. The majority of CD4⁺ T cell clones responded to a relatively short segment of NS3, namely amino acids 1207-1278, suggesting that this region of NS3 is immunodominant for CD4⁺ T cells. More than 70% of those who contract HCV develop chronic infection and hepatitis, and a significant portion of them progress to cirrhosis and eventually hepatocellular carcinoma. The only approved
10 therapy at present is a 6- to 12- month course of interferon α , which leads to sustained improvement in only 20% of patients. So far, no commercial vaccine is available.

Thus, there remains a need for compositions and methods capable of promoting anti-HCV responses.

15 SUMMARY OF THE INVENTION

In one aspect, the present invention relates to isolated polypeptides comprising mutant hepatitis C ("HCV") polypeptides comprising at least portions of NS3, NS4, and NS5. In a preferred aspect, NS3 is encoded by a nucleic acid sequence having an N-terminal deletion to remove the catalytic domain. The NS mutant polypeptides can
20 include NS3, NS4s, NS4b, NS5a, NS5b or portions thereof. For example, in various embodiments, the mutant NS polypeptide comprises NS3, NS4 (NS4a and NS4b) and NS5 (NS5a and NS5b). In other embodiments, the NS polypeptide consists of NS3 and NS4 (for example, NS4a and/or NS4b) or NS3 and NS5 (for example, NS5a and/or NS5b). Other combinations of full-length or fragments of non-structural components
25 are also contemplated.

In another preferred aspect, the polypeptides further comprise a viral polypeptide that is not a non-structural HCV polypeptide. Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are preferably E, or antigenic fragments thereof, more preferably,
30 E1 or E2 of HCV. Such polypeptides need not be encoded by a natural HCV genome, and include, for example, truncated or otherwise mutant HCV polypeptides or polypeptides derived from other genomes, such as, for example, polypeptides of HBV.

Thus, the invention includes an isolated mutant non-structural ("NS") HCV polypeptide comprising a polypeptide having a mutation in the catalytic domain of NS3 that functionally disrupts the catalytic domain. The mutation can be, for example, a deletion or a substitution mutation. In certain embodiments, the mutant NS polypeptide
5 comprises NS3, NS4 and NS5. In other embodiments, the mutant NS polypeptides described herein further comprise a second viral polypeptide that is not NS3, NS4, or NS5 of HCV, for example an HCV Core polypeptide ("C"), or fragment thereof, or an HCV envelope protein ("E"), for example E1 and/or E2. In certain embodiments, C is truncated (*e.g.*, at amino acid 121).

10 In another aspect, the present invention relates to compositions comprising any of the mutant hepatitis C ("HCV") polypeptides described herein, for example polypeptides comprising at least portions of NS3, NS4, and NS5. In a preferred aspect, NS3 is encoded by a nucleic acid sequence having an N-terminal deletion to disrupt the function of the catalytic domain, for example by removing this domain. In another
15 preferred aspect, the polypeptides further comprise a viral polypeptide that is not a non-structural HCV polypeptide. Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are preferably E, or antigenic fragments thereof, more preferably, E1 or E2 of HCV. Such polypeptides need not be encoded by a natural HCV genome, and include, for example,
20 truncated or otherwise mutant HCV polypeptides or polypeptides derived from other genomes, such as, for example, polypeptides of HBV. In another aspect, the invention includes a composition comprising (a) any of the polypeptides described herein; and (b) a pharmaceutically acceptable excipient (*e.g.*, carrier and/or adjuvant).

In another aspect, the invention includes an isolated and purified polynucleotide
25 which encodes any of the mutant HCV polypeptides described herein. In certain embodiments, the invention includes a composition comprising (a) the isolated purified polynucleotide encoding any of the mutant HCV polypeptides; and (b) a pharmaceutically acceptable excipient. The polynucleotide, can be for example, DNA in a plasmid, or is in a plasmid. Additionally, the polynucleotides described herein may
30 be included in an expression vector as shown in the attached Figures and Sequence Listings.

In another aspect, the present invention relates to host cells transformed with expression vectors comprising a nucleic acid sequence encoding a mutant HCV polypeptide comprising at least portions of NS3, NS4, and NS5. In a preferred aspect, the expression vectors of the host cells further comprises at least one nucleic acid
5 sequence encoding a viral polypeptide that is not a non-structural HCV polypeptide. Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are preferably E, or antigenic fragments thereof, more preferably, E1 or E2 of HCV. Such polypeptides need not be encoded by a natural HCV genome, and include, for example, truncated or otherwise mutant
10 HCV polypeptides or polypeptides derived from other genomes, such as, for example, polypeptides of HBV. In another preferred aspect the nucleic acid sequences of the expression vectors are coexpressed. In yet another preferred aspect, the host cells are yeast cells or mammalian cells.

In another aspect, the present invention relates to expression vectors comprising
15 a nucleic acid sequence encoding a mutant HCV polypeptide comprising NS3, NS4, and NS5. In a preferred aspect, the expression vectors of the host cells further comprises at least one nucleic acid sequence encoding a viral polypeptide that is not a non-structural HCV polypeptide. Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are
20 preferably E, or antigenic fragments thereof, more preferably, E1 or E2 of HCV. Importantly, such polypeptides need not be encoded by a natural HCV genome, such as, for example, truncated or otherwise mutant HCV polypeptides or polypeptides derived from other genomes, such as, for example, polypeptides of HBV. In another aspect, the present invention relates to methods of preparing a mutant HCV
25 polypeptides. In a preferred aspect, the method comprises the steps of transforming a host cell with an expression vector, said vector comprising a nucleic acid sequence encoding a mutant HCV polypeptide comprising at least portions of NS3, NS4, and NS5, and isolating said polypeptide. In another preferred aspect the HCV polypeptide further comprises a viral polypeptide that is not a non-structural HCV polypeptide.
30 Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are preferably E, or antigenic fragments thereof, more preferably, E1 or E2 of HCV. Such polypeptides need not be encoded by

a natural HCV genome, and include, for example, truncated or otherwise mutant HCV polypeptides or polypeptides derived from other genomes, such as, for example, polypeptides of HBV. In another preferred aspect the host cells are yeast cells or mammalian cells.

5 In another aspect, the present invention relates to antibodies which specifically bind to mutant HCV polypeptide comprising NS3, NS4, and NS5, and to methods of making and using the same. In a preferred aspect, the HCV polypeptide further comprises a viral polypeptide that is not a non-structural HCV polypeptide. Such polypeptides are preferably C, or antigenic fragments thereof, more preferably, truncated C of HCV. Other polypeptides are preferably E, or antigenic fragments thereof, more preferably, E1 or E2 of HCV. Such polypeptides need not be encoded by a natural HCV genome, such as, for example, truncated or otherwise mutant HCV polypeptides or polypeptides derived from other genomes, and include, for example, polypeptides of HBV. In another preferred aspect, the antibody is either monoclonal or polyclonal.

15 In yet another aspect, a method of preparing a mutant NS HCV polypeptide, wherein the method comprises the steps of (a) transforming a host cell with any of the expression vectors described herein, under conditions wherein the polypeptide is expressed; and (b) isolating the polypeptide. The host cell can be, for example, a yeast cell, a mammalian cell a plant cell or an insect cell. The polypeptide can be expressed and isolated intracellularly or can be secreted and isolated from the surrounding environment.

20 In a still further aspect, a method of eliciting an immune response in a subject is provided. The immune response can be elicited by administering any of the polynucleotides and/or polypeptides described herein in one or multiple doses.

25 These and other embodiments of the subject invention will readily occur to those of skill in the art in light of the disclosure herein.

BRIEF DESCRIPTION OF THE FIGURES

30 FIG. 1 shows the cloning scheme for generating pCMV-NS35.
FIG. 2 shows the 9621bp vector pCMV-NS35.

FIG. 3 shows the nucleic acid sequence of pCMV-NS35 (SEQ ID NO:1), including the nucleic acid sequence of the NS35 ORF, and also the translation of NS35 (SEQ ID NO:2).

FIG. 4 shows the 9621bp pCMV-delNS35.

- 5 FIG. 5 shows the nucleic acid sequence of pCMV-delNS35 (SEQ ID NO:3), including the nucleic acid sequence of the delNS35 ORF, and also the translation of the delNS35 polypeptide (SEQ ID NO:4).

FIG. 6 shows the 4276bp pCMV-II.

FIG. 7 shows the nucleic acid sequence of pCMV-II (SEQ ID NO:5).

- 10 FIG. 8 shows the 6300bp pCMV-NS34A.

FIG. 9 shows the nucleic acid sequence of pCMV-NS34A (SEQ ID NO:6), including the nucleic acid sequence of the NS34A ORF, and also the translation of NS34A (SEQ ID NO:7).

FIG. 10 shows the cloning scheme for generating pd.ΔNS3NS5.

- 15 FIG. 11 shows the nucleic and amino acid sequences of pd.ΔNS3NS5 (SEQ ID NO:8 and 9).

FIG. 12 shows the Western blot of proteins expressed by *S. cerevisiae* strain AD3 transformed with pd.ΔNS3NS5.

FIG. 13 shows the cloning scheme for generating pd.ΔNS3NS5.pj.

- 20 FIG. 14 shows the nucleic and amino acid sequences of pd.ΔNS3NS5.pj (SEQ ID NO:10 and 11).

FIG. 15 shows the Western blot of proteins expressed by *S. cerevisiae* strain AD3 transformed with pd.ΔNS3NS5.pj, specifically demonstrating the expression of ΔNS3NS5 polypeptide.

- 25 FIG. 16 shows the cloning scheme for generating pdΔNS3NS5.pj.core121RT and pdΔNS3NS5.pj.core173RT.

FIG. 17 shows the nucleic and amino acid sequences of pd.ΔNS3NS5.pj.core121 (SEQ ID NO:12 and 13).

- 30 FIG. 18 shows the nucleic and amino acid sequences of pd.ΔNS3NS5.pj.core173 (SEQ ID NO:14 and 15).

FIG. 19 shows the Western blot of proteins expressed by *S. cerevisiae* strain AD3 transformed with pd.ΔNS3NS5.pj, specifically demonstrating the expression of

Δ NS3NS5.core121 and Δ NS3NS5.core173 polypeptides. Lanes 1 and 7 show See Blue Standards. Lane 2 shows control yeast plasmid. Lanes 3 and 4 show Δ NS3NS5.core121RT polypeptide, colonies 1 and 2. Lanes 5 and 6 show Δ NS3NS5.core173RT polypeptide, colonies 3 and 4.

- 5 FIG. 20 shows the cloning scheme for generating pd Δ NS3NS5.pj.core140RT and pd Δ NS3NS5.pj.core150RT.
- FIG. 21 shows the nucleic and amino acid sequences of pd. Δ NS3NS5.pj.core140 (SEQ ID NO:16 and 17).
- FIG. 22 shows the nucleic and amino acid sequences of pd. Δ NS3NS5.pj.core150 (SEQ
- 10 ID NO:18 and 19).
- FIG. 23 shows the Western blot of proteins expressed by *S. cerevisiae* strain AD3 transformed with pd. Δ NS3NS5.pj, specifically demonstrating the expression of Δ NS3NS5core140 and Δ NS3NS5core150 polypeptides. Lane 1 shows See Blue Standards. Lanes 2 and 3 show Δ NS3NS5core140RT polypeptide, colonies 5 and 6.
- 15 Lanes 4 and 5 show Δ NS3NS5core150RT polypeptide, colonies 7 and 8. Lane 6 shows control yeast plasmid. Lane 7 shows Δ NS3NS5core121RT polypeptide, colony 1. Lane 8 shows Δ NS3NS5core173RT polypeptide, colony 5.

DETAILED DESCRIPTION OF THE INVENTION

- 20 The practice of the present invention will employ, unless otherwise indicated, conventional techniques of molecular biology, microbiology, recombinant DNA techniques, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. See e.g., Sambrook, et al., MOLECULAR CLONING; A LABORATORY MANUAL (1989); DNA CLONING, VOLUMES I AND II (D. N.
- 25 Glover ed. 1985); OLIGONUCLEOTIDE SYNTHESIS (M. J. Gait ed., 1984); NUCLEIC ACID HYBRIDIZATION (B. D. Hames & S. J. Higgins eds. 1984); TRANSCRIPTION AND TRANSLATION (B. D. Hames & S. J. Higgins eds. 1984); ANIMAL CELL CULTURE (R. I. Freshney ed. 1986); IMMOBILIZED CELLS AND ENZYMES (IRL Press, 1986); B. Perbal, A PRACTICAL GUIDE TO MOLECULAR
- 30 CLONING (1984); the series, METHODS OF ENZYMOLOGY (Academic Press, Inc.); GENE TRANSFER VECTORS FOR MAMMALIAN CELLS (J. H. Miller and M. P. Calos eds. 1987, Cold Springs Harbor Laboratory), Methods in Enzymology Vol.

154 and Vol. 155 (Wu and Grossman, and Wu, eds., respectively); Mayer and Walker
eds. (1987), IMMUNOHISTOCHEMICAL METHODS IN CELL AND
MOLECULAR BIOLOGY (Academic Press, London); Scopes, (1987), PROTEIN
PURIFICATION: PRINCIPALS AND PRACTICE, Second Edition (Springer-Verlag,
5 New York); and HANDBOOK OF EXPERIMENTAL IMMUNOLOGY, VOLUMES
I-IV (D. M. Weir and C. C. Blackwell eds. 1986).

It must be noted that, as used in this specification and the appended claims, the
singular forms "a", "an" and "the" include plural referents unless the content clearly
dictates otherwise. Thus, for example, reference to "an antigen" includes a mixture of
10 two or more antigens, and the like.

I. Definitions

In describing the present invention, the following terms will be employed, and
are intended to be defined as indicated below.

15 The term "hepatitis C virus" (HCV) refers to an agent causative of Non-A, Non-
B Hepatitis (NANBH). The nucleic acid sequence and putative amino acid sequence of
HCV is described in U.S. Patent Nos. 5,856,437 and 5,350,671. The disease caused by
HCV is called hepatitis C, formerly called NANBH. The term HCV, as used herein,
denotes a viral species of which pathenogenic strains cause NANBH, as well as
20 attenuated strains or defective interfering particles derived therefrom.

HCV is a member of the viral family flaviviridae. The morphology and
composition of Flavivirus particles are known, and are discussed in Reed et al., *Curr.*
Stud. Hematol. Blood Transfus. (1998), 62:1-37; HEPATITIS C VIRUSES IN FIELDS
VIROLOGY (B.N. Fields, D.M. Knipe, P.M. Howley, eds.) (3d ed. 1996). It has
25 recently been found that portions of the HCV genome are also homologous to
pestiviruses. Generally, with respect to morphology, Flaviviruses contain a central
nucleocapsid surrounded by a lipid bilayer. Virions are spherical and have a diameter
of about 40-50 nm. Their cores are about 25-30 nm in diameter. Along the outer
surface of the virion envelope are projections that are about 5-10 nm long with terminal
30 knobs about 2 nm in diameter.

The HCV genome is comprised of RNA. It is known that RNA containing
viruses have relatively high rates of spontaneous mutation. Therefore, there can be

multiple strains, which can be virulent or avirulent, within the HCV class or species. The ORF of HCV, including the translation spans of the core, non-structural, and envelope proteins, is shown in U.S. Patent Nos. 5,856,437 and 5,350,671.

The terms "polypeptide" and "protein" refer to a polymer of amino acid residues and are not limited to a minimum length of the product. Thus, peptides, oligopeptides, dimers, multimers, and the like, are included within the definition. Both full-length proteins and fragments thereof are encompassed by the definition. The terms also include postexpression modifications of the polypeptide, for example, glycosylation, acetylation, phosphorylation and the like. Furthermore, for purposes of the present invention, a "polypeptide" refers to a protein which includes modifications, such as deletions, additions and substitutions (generally conservative in nature), to the native sequence, so long as the protein maintains the desired activity. These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental, such as through mutations of hosts which produce the proteins or errors due to PCR amplification.

An HCV polypeptide is a polypeptide, as defined above, derived from the HCV polyprotein. The polypeptide need not be physically derived from HCV, but may be synthetically or recombinantly produced. Moreover, the polypeptide may be derived from any of the various HCV strains, such as from strains 1, 2, 3 or 4 of HCV. A number of conserved and variable regions are known between these strains and, in general, the amino acid sequences of epitopes derived from these regions will have a high degree of sequence homology, e.g., amino acid sequence homology of more than 30%, preferably more than 40%, when the two sequences are aligned and homology determined by any of the programs or algorithms described herein. Thus, for example, the term "NS4" polypeptide refers to native NS4 from any of the various HCV strains, as well as NS4 analogs, muteins and immunogenic fragments, as defined further below.

Further, the terms " Δ NS35," "delNS35," " Δ NS3NS5," and " Δ NS3-5" as used herein refer to a mutant polypeptide, comprising at least portions of NS3, NS4, or NS5, comprising a deletion in, or mutation of, the NS3 protease active site region to render the protease non-functional. In one embodiment, Δ NS3-5 comprises amino acids 1242-3011, as shown in FIG. 5, or polypeptides substantially homologous thereto. It will be readily apparent to one of ordinary skill in the art how to determine that NS3 protease

has been rendered non-functional. If the protease is functional, one will obtain protein of the expected molecular weight upon expression. As set forth in Example 2 and Figure 15, using SDS-page, 4-20%, a protein having a molecular weight of approximately 194kD was obtained when strain AD3 was transformed with
5 pd.ANS3NS5.PJ clone #5. One skilled in the art could readily determine whether a protein of the desired molecular weight was expressed for any given deletion or mutation.

The terms "analog" and "mutein" refer to biologically active derivatives of the reference molecule, or fragments of such derivatives, that retain desired activity, such
10 as the ability to stimulate a cell-mediated immune response, as defined below. In general, the term "analog" refers to compounds having a native polypeptide sequence and structure with one or more amino acid additions, substitutions (generally conservative in nature) and/or deletions, relative to the native molecule, so long as the modifications do not destroy immunogenic activity. The term "mutein" refers to
15 peptides having one or more peptide mimics ("peptoids"), such as those described in International Publication No. WO 91/04282. Preferably, the analog or mutein has at least the same immunoactivity as the native molecule. Methods for making polypeptide analogs and muteins are known in the art and are described further below.

Particularly preferred analogs include substitutions that are conservative in
20 nature, i.e., those substitutions that take place within a family of amino acids that are related in their side chains. Specifically, amino acids are generally divided into four families: (1) acidic -- aspartate and glutamate; (2) basic -- lysine, arginine, histidine; (3) non-polar -- alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar -- glycine, asparagine, glutamine, cysteine, serine
25 threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified as aromatic amino acids. For example, it is reasonably predictable that an isolated replacement of leucine with isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar conservative replacement of an amino acid with a structurally related amino acid, will not have a major effect on the biological activity.
30 For example, the polypeptide of interest may include up to about 5-10 conservative or non-conservative amino acid substitutions, or even up to about 15-25 conservative or non-conservative amino acid substitutions, or any integer between 5-25, so long as the

desired function of the molecule remains intact. One of skill in the art may readily determine regions of the molecule of interest that can tolerate change by reference to Hopp/Woods and Kyte-Doolittle plots, well known in the art.

By "fragment" is intended a polypeptide consisting of only a part of the intact
5 full-length polypeptide sequence and structure. The fragment can include a C-terminal deletion and/or an N-terminal deletion of the native polypeptide. An "immunogenic fragment" of a particular HCV protein will generally include at least about 5-10 contiguous amino acid residues of the full-length molecule, preferably at least about 15-25 contiguous amino acid residues of the full-length molecule, and most preferably
10 at least about 20-50 or more contiguous amino acid residues of the full-length molecule, that define an epitope, or any integer between 5 amino acids and the full-length sequence, provided that the fragment in question retains immunogenic activity, as measured by the assays described herein. For a description of various HCV epitopes, see, e.g., Chien et al., *Proc. Natl. Acad. Sci. USA* (1992) 89:10011-10015;
15 Chien et al., *J. Gastroent. Hepatol.* (1993) 8:S33-39; Chien et al., International Publication No. WO 93/00365; Chien, D.Y., International Publication No. WO 94/01778; commonly owned, allowed U.S. Patent Application Serial Nos. 08/403,590 and 08/444,818.

The term "epitope" as used herein refers to a sequence of at least about 3 to 5,
20 preferably about 5 to 10 or 15, and not more than about 1,000 amino acids (or any integer therebetween); which define a sequence that by itself or as part of a larger sequence, binds to an antibody generated in response to such sequence. There is no critical upper limit to the length of the fragment, which may comprise nearly the full-length of the protein sequence, or even a fusion protein comprising two or more
25 epitopes from the HCV polyprotein. An epitope for use in the subject invention is not limited to a polypeptide having the exact sequence of the portion of the parent protein from which it is derived. Indeed, viral genomes are in a state of constant flux and contain several variable domains which exhibit relatively high degrees of variability between isolates. Thus the term "epitope" encompasses sequences identical to the
30 native sequence, as well as modifications to the native sequence, such as deletions, additions and substitutions (generally conservative in nature).

Regions of a given polypeptide that include an epitope can be identified using any number of epitope mapping techniques, well known in the art. See, e.g., *Epitope Mapping Protocols* in *Methods in Molecular Biology*, Vol. 66 (Glenn E. Morris, Ed., 1996) Humana Press, Totowa, New Jersey. For example, linear epitopes may be
5 determined by e.g., concurrently synthesizing large numbers of peptides on solid supports, the peptides corresponding to portions of the protein molecule, and reacting the peptides with antibodies while the peptides are still attached to the supports. Such techniques are known in the art and described in, e.g., U.S. Patent No. 4,708,871; Geysen et al. (1984) *Proc. Natl. Acad. Sci. USA* 81:3998-4002; Geysen et al. (1986)
10 *Molec. Immunol.* 23:709-715. Similarly, conformational epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., x-ray crystallography and 2-dimensional nuclear magnetic resonance. See, e.g., *Epitope Mapping Protocols*, *supra*. Antigenic regions of proteins can also be identified using standard antigenicity and hydropathy plots, such as those calculated using, e.g., the
15 Omega version 1.0 software program available from the Oxford Molecular Group. This computer program employs the Hopp/Woods method, Hopp et al., *Proc. Natl. Acad. Sci USA* (1981) 78:3824-3828 for determining antigenicity profiles, and the Kyte-Doolittle technique, Kyte et al., *J. Mol. Biol.* (1982) 157:105-132 for hydropathy plots.

As used herein, the term "conformational epitope" refers to a portion of a full-
20 length protein, or an analog or mutein thereof, having structural features native to the amino acid sequence encoding the epitope within the full-length natural protein. Native structural features include, but are not limited to, glycosylation and three dimensional structure. Preferably, a conformational epitope is produced recombinantly and is expressed in a cell from which it is extractable under conditions which preserve its
25 desired structural features, e.g. without denaturation of the epitope. Such cells include bacteria, yeast, insect, and mammalian cells. Expression and isolation of recombinant conformational epitopes from the HCV polyprotein are described in e.g., International Publication Nos. WO 96/04301, WO 94/01778, WO 95/33053, WO 92/08734.

An "immunological response" to an HCV antigen (including both polypeptide
30 and polynucleotides encoding polypeptides that are expressed *in vivo*) or composition is the development in a subject of a humoral and/or a cellular immune response to molecules present in the composition of interest. For purposes of the present invention,

a "humoral immune response" refers to an immune response mediated by antibody molecules, while a "cellular immune response" is one mediated by T-lymphocytes and/or other white blood cells. One important aspect of cellular immunity involves an antigen-specific response by cytolytic T-cells ("CTLs"). CTLs have specificity for peptide antigens that are presented in association with proteins encoded by the major histocompatibility complex (MHC) and expressed on the surfaces of cells. CTLs help induce and promote the intracellular destruction of intracellular microbes, or the lysis of cells infected with such microbes. Another aspect of cellular immunity involves an antigen-specific response by helper T-cells. Helper T-cells act to help stimulate the function, and focus the activity of, nonspecific effector cells against cells displaying peptide antigens in association with MHC molecules on their surface. A "cellular immune response" also refers to the production of cytokines, chemokines and other such molecules produced by activated T-cells and/or other white blood cells, including those derived from CD4+ and CD8+ T-cells.

A composition or vaccine that elicits a cellular immune response may serve to sensitize a vertebrate subject by the presentation of antigen in association with MHC molecules at the cell surface. The cell-mediated immune response is directed at, or near, cells presenting antigen at their surface. In addition, antigen-specific T-lymphocytes can be generated to allow for the future protection of an immunized host.

The ability of a particular antigen to stimulate a cell-mediated immunological response may be determined by a number of assays, such as by lymphoproliferation (lymphocyte activation) assays, CTL cytotoxic cell assays, or by assaying for T-lymphocytes specific for the antigen in a sensitized subject. Such assays are well known in the art. See, e.g., Erickson et al., *J. Immunol.* (1993) 151:4189-4199; Doe et al., *Eur. J. Immunol.* (1994) 24:2369-2376; and the examples below.

Thus, an immunological response as used herein may be one which stimulates the production of CTLs, and/or the production or activation of helper T-cells. The antigen of interest may also elicit an antibody-mediated immune response. Hence, an immunological response may include one or more of the following effects: the production of antibodies by B-cells; and/or the activation of suppressor T-cells and/or $\gamma\delta$ T-cells directed specifically to an antigen or antigens present in the composition or vaccine of interest. These responses may serve to neutralize infectivity, and/or mediate

antibody-complement, or antibody dependent cell cytotoxicity (ADCC) to provide protection or alleviation of symptoms to an immunized host. Such responses can be determined using standard immunoassays and neutralization assays, well known in the art.

5 A "coding sequence" or a sequence which "encodes" a selected polypeptide, is a nucleic acid molecule which is transcribed (in the case of DNA) and translated (in the case of mRNA) into a polypeptide *in vitro* or *in vivo* when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a start codon at the 5' (amino) terminus and a translation stop codon at
10 the 3' (carboxy) terminus. A transcription termination sequence may be located 3' to the coding sequence.

 A "nucleic acid" molecule or "polynucleotide" can include both double- and single-stranded sequences and refers to, but is not limited to, cDNA from viral, procaryotic or eucaryotic mRNA, genomic DNA sequences from viral (e.g. DNA
15 viruses and retroviruses) or procaryotic DNA, and especially synthetic DNA sequences. The term also captures sequences that include any of the known base analogs of DNA and RNA.

 "Operably linked" refers to an arrangement of elements wherein the components so described are configured so as to perform their desired function. Thus,
20 a given promoter operably linked to a coding sequence is capable of effecting the expression of the coding sequence when the proper transcription factors, etc., are present. The promoter need not be contiguous with the coding sequence, so long as it functions to direct the expression thereof. Thus, for example, intervening untranslated yet transcribed sequences can be present between the promoter sequence and the coding
25 sequence, as can transcribed introns, and the promoter sequence can still be considered "operably linked" to the coding sequence.

 "Recombinant" as used herein to describe a nucleic acid molecule means a polynucleotide of genomic, cDNA, viral, semisynthetic, or synthetic origin which, by virtue of its origin or manipulation is not associated with all or a portion of the
30 polynucleotide with which it is associated in nature. The term "recombinant" as used with respect to a protein or polypeptide means a polypeptide produced by expression of a recombinant polynucleotide. In general, the gene of interest is cloned and then

expressed in transformed organisms, as described further below. The host organism expresses the foreign gene to produce the protein under expression conditions.

5 A "control element" refers to a polynucleotide sequence which aids in the expression of a coding sequence to which it is linked. The term includes promoters, transcription termination sequences, upstream regulatory domains, polyadenylation signals, untranslated regions, including 5'-UTRs and 3'-UTRs and when appropriate, leader sequences and enhancers, which collectively provide for the transcription and translation of a coding sequence in a host cell.

10 A "promoter" as used herein is a DNA regulatory region capable of binding RNA polymerase in a host cell and initiating transcription of a downstream (3' direction) coding sequence operably linked thereto. For purposes of the present invention, a promoter sequence includes the minimum number of bases or elements necessary to initiate transcription of a gene of interest at levels detectable above background. Within the promoter sequence is a transcription initiation site, as well as
15 protein binding domains (consensus sequences) responsible for the binding of RNA polymerase. Eucaryotic promoters will often, but not always, contain "TATA" boxes and "CAT" boxes.

A control sequence "directs the transcription" of a coding sequence in a cell when RNA polymerase will bind the promoter sequence and transcribe the coding
20 sequence into mRNA, which is then translated into the polypeptide encoded by the coding sequence.

"Expression cassette" or "expression construct" refers to an assembly which is capable of directing the expression of the sequence(s) or gene(s) of interest. The expression cassette includes control elements, as described above, such as a promoter
25 which is operably linked to (so as to direct transcription of) the sequence(s) or gene(s) of interest, and often includes a polyadenylation sequence as well. Within certain embodiments of the invention, the expression cassette described herein may be contained within a plasmid construct. In addition to the components of the expression cassette, the plasmid construct may also include, one or more selectable markers, a
30 signal which allows the plasmid construct to exist as single-stranded DNA (e.g., a M13 origin of replication), at least one multiple cloning site, and a "mammalian" origin of replication (e.g., a SV40 or adenovirus origin of replication).

“Transformation,” as used herein, refers to the insertion of an exogenous polynucleotide into a host cell, irrespective of the method used for insertion: for example, transformation by direct uptake, transfection, infection, and the like. For particular methods of transfection, see further below. The exogenous polynucleotide
5 may be maintained as a nonintegrated vector, for example, an episome, or alternatively, may be integrated into the host genome.

A “host cell” is a cell which has been transformed, or is capable of transformation, by an exogenous DNA sequence.

By “isolated” is meant, when referring to a polypeptide, that the indicated
10 molecule is separate and discrete from the whole organism with which the molecule is found in nature or is present in the substantial absence of other biological macromolecules of the same type. The term “isolated” with respect to a polynucleotide is a nucleic acid molecule devoid, in whole or part, of sequences normally associated with it in nature; or a sequence, as it exists in nature, but having heterologous sequences in
15 association therewith; or a molecule disassociated from the chromosome.

The term “purified” as used herein preferably means at least 75% by weight, more preferably at least 85% by weight, more preferably still at least 95% by weight, and most preferably at least 98% by weight, of biological macromolecules of the same type are present.

20 “Homology” refers to the percent identity between two polynucleotide or two polypeptide moieties. Two DNA, or two polypeptide sequences are “substantially homologous” to each other when the sequences exhibit at least about 50% , preferably at least about 75%, more preferably at least about 80%-85%, preferably at least about 90%, and most preferably at least about 95%-98%, or more, sequence identity over a
25 defined length of the molecules. As used herein, substantially homologous also refers to sequences showing complete identity to the specified DNA or polypeptide sequence. The term “substantially homologous” as used herein in reference to ΔNS35 generally refers to an HCV nucleic or amino acid sequence that is at least 60% identical to the entire sequence of the polypeptide encoded by ΔNS35 (see FIG. 5), where the sequence
30 identity is preferably at least 75%, more preferably at least 80%, still more preferably at least about 85%, especially more than about 90%, most preferably 95% or greater, particularly 98% or greater. These homologous polypeptides include fragments,

including mutants and allelic variants of the fragments. Identity between the two sequences is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affine gap search with parameters *gap open penalty*=12 and *gap extension penalty*=1. Thus, for
5 example, the present invention includes an isolate which is 80% identical to a polypeptide encoded by Δ NS35. In some aspects of the invention, the polypeptide of the present invention is substantially homologous to the Δ NS35.

In general, "identity" refers to an exact nucleotide-to-nucleotide or amino acid-to-amino acid correspondence of two polynucleotides or polypeptide sequences,
10 respectively. Percent identity can be determined by a direct comparison of the sequence information between two molecules by aligning the sequences, counting the exact number of matches between the two aligned sequences, dividing by the length of the shorter sequence, and multiplying the result by 100. Readily available computer programs can be used to aid in the analysis, such as ALIGN, Dayhoff, M.O. in *Atlas of*
15 *Protein Sequence and Structure* M.O. Dayhoff ed., 5 Suppl. 3:353-358, National biomedical Research Foundation, Washington, DC, which adapts the local homology algorithm of Smith and Waterman *Advances in Appl. Math.* 2:482-489, 1981 for peptide analysis. Programs for determining nucleotide sequence identity are available in the Wisconsin Sequence Analysis Package, Version 8 (available from Genetics
20 Computer Group, Madison, WI) for example, the BESTFIT, FASTA and GAP programs, which also rely on the Smith and Waterman algorithm. These programs are readily utilized with the default parameters recommended by the manufacturer and described in the Wisconsin Sequence Analysis Package referred to above. For example, percent identity of a particular nucleotide sequence to a reference sequence
25 can be determined using the homology algorithm of Smith and Waterman with a default scoring table and a gap penalty of six nucleotide positions.

Another method of establishing percent identity in the context of the present invention is to use the MPSRCH package of programs copyrighted by the University of Edinburgh, developed by John F. Collins and Shane S. Sturrok, and distributed by
30 IntelliGenetics, Inc. (Mountain View, CA). From this suite of packages the Smith-Waterman algorithm can be employed where default parameters are used for the scoring table (for example, gap open penalty of 12, gap extension penalty of one, and a

gap of six). From the data generated the "Match" value reflects "sequence identity." Other suitable programs for calculating the percent identity or similarity between sequences are generally known in the art, for example, another alignment program is BLAST, used with default parameters. For example, BLASTN and BLASTP can be
5 used using the following default parameters: genetic code = standard; filter = none; strand = both; cutoff = 60; expect = 10; Matrix = BLOSUM62; Descriptions = 50 sequences; sort by = HIGH SCORE; Databases = non-redundant, GenBank + EMBL + DDBJ + PDB + GenBank CDS translations + Swiss protein + Spupdate + PIR. Details of these programs can be found at the following internet address:

10 <http://www.ncbi.nlm.gov/cgi-bin/BLAST>.

Alternatively, homology can be determined by hybridization of polynucleotides under conditions which form stable duplexes between homologous regions, followed by digestion with single-stranded-specific nuclease(s), and size determination of the digested fragments. DNA sequences that are substantially homologous can be
15 identified in a Southern hybridization experiment under, for example, stringent conditions, as defined for that particular system. Defining appropriate hybridization conditions is within the skill of the art. See, e.g., Sambrook et al., *supra*; *DNA Cloning, supra*; *Nucleic Acid Hybridization, supra*.

"Stringency" refers to conditions in a hybridization reaction that favor
20 association of very similar sequences over sequences that differ. For example, the combination of temperature and salt concentration should be chosen that is approximately 120 to 200°C below the calculated T_m of the hybrid under study. The temperature and salt conditions can often be determined empirically in preliminary experiments in which samples of genomic DNA immobilized on filters are hybridized
25 to the sequence of interest and then washed under conditions of different stringencies. See Sambrook *et al.* at page 9.50.

Variables to consider when performing, for example, a Southern blot are (1) the complexity of the DNA being blotted and (2) the homology between the probe and the sequences being detected. The total amount of the fragment(s) to be studied can vary a
30 magnitude of 10, from 0.1 to 1 µg for a plasmid or phage digest to 10⁻⁹ to 10⁻⁸ g for a single copy gene in a highly complex eukaryotic genome. For lower complexity polynucleotides, substantially shorter blotting, hybridization, and exposure times, a

smaller amount of starting polynucleotides, and lower specific activity of probes can be used. For example, a single-copy yeast gene can be detected with an exposure time of only 1 hour starting with 1 µg of yeast DNA, blotting for two hours, and hybridizing for 4-8 hours with a probe of 10^8 cpm/µg. For a single-copy mammalian gene a
5 conservative approach would start with 10 µg of DNA, blot overnight, and hybridize overnight in the presence of 10% dextran sulfate using a probe of greater than 10^8 cpm/µg, resulting in an exposure time of ~24 hours.

Several factors can affect the melting temperature (T_m) of a DNA-DNA hybrid between the probe and the fragment of interest, and consequently, the appropriate
10 conditions for hybridization and washing. In many cases the probe is not 100% homologous to the fragment. Other commonly encountered variables include the length and total G+C content of the hybridizing sequences and the ionic strength and formamide content of the hybridization buffer. The effects of all of these factors can be approximated by a single equation:

15 $T_m = 81 + 16.6(\log_{10}Ci) + 0.4[\%(G + C)] - 0.6(\%\text{formamide}) - 600/n - 1.5(\%\text{mismatch})$.
where Ci is the salt concentration (monovalent ions) and n is the length of the hybrid in base pairs (slightly modified from Meinkoth & Wahl (1984) *Anal. Biochem.* 138: 267-284). In general, convenient hybridization temperatures in the presence of 50% formamide are 42°C for a probe with is 95% to 100% homologous to the target
20 fragment, 37°C for 90% to 95% homology, and 32°C for 85% to 90% homology. For lower homologies, formamide content should be lowered and temperature adjusted accordingly, using the equation above. If the homology between the probe and the target fragment are not known, the simplest approach is to start with both hybridization and wash conditions which are nonstringent. If non-specific bands or high background
25 are observed after autoradiography, the filter can be washed at high stringency and reexposed. If the time required for exposure makes this approach impractical, several hybridization and/or washing stringencies should be tested in parallel.

By "nucleic acid immunization" is meant the introduction of a nucleic acid molecule encoding one or more selected antigens into a host cell, for the *in vivo*
30 expression of the antigen or antigens. The nucleic acid molecule can be introduced directly into the recipient subject, such as by injection, inhalation, oral, intranasal and mucosal administration, or the like, or can be introduced *ex vivo*, into cells which have

been removed from the host. In the latter case, the transformed cells are reintroduced into the subject where an immune response can be mounted against the antigen encoded by the nucleic acid molecule.

5 An "open reading frame" or ORF is a region of a polynucleotide sequence which encodes a polypeptide; this region can represent a portion of a coding sequence or a total coding sequence.

10 As used herein, the term "antibody" refers to a polypeptide or group of polypeptides which comprise at least one antigen binding site. An "antigen binding site" is formed from the folding of the variable domains of an antibody molecule(s) to form three-dimensional binding sites with an internal surface shape and charge distribution complementary to the features of an epitope of an antigen, which allows specific binding to form an antibody-antigen complex. An antigen binding site may be formed from a heavy- and/or light-chain domain (VH and VL, respectively), which form hypervariable loops which contribute to antigen binding. The term "antibody" 15 includes, without limitation, polyclonal antibodies, monoclonal antibodies, chimeric antibodies, altered antibodies, univalent antibodies, Fab proteins, and single-domain antibodies. In many cases, the binding phenomena of antibodies to antigens is equivalent to other ligand/anti-ligand binding.

20 If polyclonal antibodies are desired, a selected mammal (e.g., mouse, rabbit, goat, horse, etc.) is immunized with an immunogenic polypeptide bearing an HCV epitope(s). Serum from the immunized animal is collected and treated according to known procedures. If serum containing polyclonal antibodies to an HCV epitope contains antibodies to other antigens, the polyclonal antibodies can be purified by immunoaffinity chromatography. Techniques for producing and processing polyclonal antisera are known in the art, see for example, Mayer and Walker, eds. (1987) 25 IMMUNOCHEMICAL METHODS IN CELL AND MOLECULAR BIOLOGY (Academic Press, London).

30 Monoclonal antibodies directed against HCV epitopes can also be readily produced by one skilled in the art. The general methodology for making monoclonal antibodies by hybridomas is well known. Immortal antibody-producing cell lines can be created by cell fusion, and also by other techniques such as direct transformation of B lymphocytes with oncogenic DNA, or transfection with Epstein-Barr virus. See, e.g.,

M. Schreier et al. (1980) HYBRIDOMA TECHNIQUES; Hammerling et al. (1981), MONOCLONAL ANTIBODIES AND T-CELL HYBRIDOMAS; Kennett et al. (1980) MONOCLONAL ANTIBODIES; see also, U.S. Pat. Nos. 4,341,761; 4,399,121; 4,427,783; 4,444,887; 4,466,917; 4,472,500; 4,491,632; and 4,493,890. Panels of
5 monoclonal antibodies produced against HCV epitopes can be screened for various properties; i.e., for isotype, epitope affinity, etc. As used herein, a "single domain antibody" (dAb) is an antibody which is comprised of an HL domain, which binds specifically with a designated antigen. A dAb does not contain a VL domain, but may contain other antigen binding domains known to exist to antibodies, for example, the
10 kappa and lambda domains. Methods for preparing dabs are known in the art. See, for example, Ward et al, Nature 341: 544 (1989).

Antibodies can also be comprised of VH and VL domains, as well as other known antigen binding domains. Examples of these types of antibodies and methods for their preparation and known in the art (see, e.g., U.S. Pat. No. 4,816,467), and
15 include the following. For example, "vertebrate antibodies" refers to antibodies which are tetramers or aggregates thereof, comprising light and heavy chains which are usually aggregated in a "Y" configuration and which may or may not have covalent linkages between the chains. In vertebrate antibodies, the amino acid sequences of the chains are homologous with those sequences found in antibodies produced in
20 vertebrates, whether in situ or in vitro (for example, in hybridomas). Vertebrate antibodies include, for example, purified polyclonal antibodies and monoclonal antibodies, methods for the preparation of which are described infra.

"Hybrid antibodies" are antibodies where chains are separately homologous with reference to mammalian antibody chains and represent novel assemblies of them,
25 so that two different antigens are precipitable by the tetramer or aggregate. In hybrid antibodies, one pair of heavy and light chains are homologous to those found in an antibody raised against a first antigen, while a second pair of chains are homologous to those found in an antibody raised against a second antibody. This results in the property of "divalence", i.e., the ability to bind two antigens simultaneously. Such hybrids can
30 also be formed using chimeric chains, as set forth below.

"Chimeric antibodies" refers to antibodies in which the heavy and/or light chains are fusion proteins. Typically, one portion of the amino acid sequences of the

chain is homologous to corresponding sequences in an antibody derived from a particular species or a particular class, while the remaining segment of the chain is homologous to the sequences derived from another species and/or class. Usually, the variable region of both light and heavy chains mimics the variable regions or antibodies
5 derived from one species of vertebrates, while the constant portions are homologous to the sequences in the antibodies derived from another species of vertebrates. However, the definition is not limited to this particular example. Also included is any antibody in which either or both of the heavy or light chains are composed of combinations of sequences mimicking the sequences in antibodies of different sources, whether these
10 sources be from differing classes or different species of origin, and whether or not the fusion point is at the variable/constant boundary. Thus, it is possible to produce antibodies in which neither the constant nor the variable region mimic known antibody sequences. It then becomes possible, for example, to construct antibodies whose variable region has a higher specific affinity for a particular antigen, or whose constant
15 region can elicit enhanced complement fixation, or to make other improvements in properties possessed by a particular constant region.

Another example is "altered antibodies", which refers to antibodies in which the naturally occurring amino acid sequence in a vertebrate antibody has been varied. Utilizing recombinant DNA techniques, antibodies can be redesigned to obtain desired
20 characteristics. The possible variations are many, and range from the changing of one or more amino acids to the complete redesign of a region, for example, the constant region. Changes in the constant region, in general, to attain desired cellular process characteristics, e.g., changes in complement fixation, interaction with membranes, and other effector functions. Changes in the variable region can be made to alter antigen
25 binding characteristics. The antibody can also be engineered to aid the specific delivery of a molecule or substance to a specific cell or tissue site. The desired alterations can be made by known techniques in molecular biology, e.g., recombinant techniques, site-directed mutagenesis, etc.

Yet another example are "univalent antibodies", which are aggregates
30 comprised of a heavy-chain/light-chain dimer bound to the Fc (i.e., stem) region of a second heavy chain. This type of antibody escapes antigenic modulation. See, e.g., Glennie et al. Nature 295: 712 (1982). Included also within the definition of antibodies

are "Fab" fragments of antibodies. The "Fab" region refers to those portions of the heavy and light chains which are roughly equivalent, or analogous, to the sequences which comprise the branch portion of the heavy and light chains, and which have been shown to exhibit immunological binding to a specified antigen, but which lack the effector Fc portion. "Fab" includes aggregates of one heavy and one light chain (commonly known as Fab'), as well as tetramers containing the 2H and 2L chains (referred to as F(ab)2), which are capable of selectively reacting with a designated antigen or antigen family. Fab antibodies can be divided into subsets analogous to those described above, i.e., "vertebrate Fab", "hybrid Fab", "chimeric Fab", and "altered Fab".

Methods of producing Fab fragments of antibodies are known within the art and include, for example, proteolysis, and synthesis by recombinant techniques.

"Antigen-antibody complex" refers to the complex formed by an antibody that is specifically bound to an epitope on an antigen.

"Immunogenic polypeptide" refers to a polypeptide that elicits a cellular and/or humoral immune response in a mammal, whether alone or linked to a carrier, in the presence or absence of an adjuvant.

"Antigenic determinant" refers to the site on an antigen or hapten to which a specific antibody molecule or specific cell surface receptor binds.

As used herein, "treatment" refers to any of (i) the prevention of infection or reinfection, as in a traditional vaccine, (ii) the reduction or elimination of symptoms, and (iii) the substantial or complete elimination of the pathogen in question. Treatment may be effected prophylactically (prior to infection) or therapeutically (following infection).

By "vertebrate subject" is meant any member of the subphylum cordata, including, without limitation, humans and other primates, including non-human primates such as chimpanzees and other apes and monkey species; farm animals such as cattle, sheep, pigs, goats and horses; domestic mammals such as dogs and cats; laboratory animals including rodents such as mice, rats and guinea pigs; birds, including domestic, wild and game birds such as chickens, turkeys and other gallinaceous birds, ducks, geese, and the like. The term does not denote a particular age. Thus, both adult and newborn individuals are intended to be covered. The

invention described herein is intended for use in any of the above vertebrate species, since the immune systems of all of these vertebrates operate similarly.

II. Modes of Carrying out the Invention

5 Before describing the present invention in detail, it is to be understood that this invention is not limited to particular formulations or process parameters as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only, and is not intended to be limiting.

10 Although a number of compositions and methods similar or equivalent to those described herein can be used in the practice of the present invention, the preferred materials and methods are described herein.

General Overview

15 An aim of an HCV vaccine is to generate broad immunity to a wide breadth of antigens because HCV is so divergent and because humoral as well as cellular immune responses are desirable to combat this human pathogen. While antibodies generated against the envelope glycoprotein(s) might aid in virus neutralization, there is additional benefit to be derived from a vaccine that includes other regions. The
20 likelihood of T-helper responses generated against a polypeptide would be helpful in a vaccine setting as would generation of cytotoxic T cells. The non-structural region represents such a candidate antigen, but processing by the protease generates several polypeptides, making purification complicated. It would be advantageous, therefore, to derive a non-structural cassette that is unprocessed by the NS3 protease.

25 The present invention solves this and other problems using compositions and methods involving an N-terminal deletion in NS3, which removes the catalytic domain. As such, some or all of the remainder of the non-structural region (through NS5B) is expressed as an intact polypeptide. Expression of this species has been documented in mammalian cells as well as in yeast. Further, in certain aspects, polynucleotides
30 encoding HCV core polypeptides (or fragments thereof) are added (*e.g.* operably linked) to the carboxy-terminus of the non-structural cassette. As the core coding region is relatively highly conserved among HCV isolates, the presence of this region

may enhance the immune response. Because core has at its C-terminus a very hydrophobic domain (amino acids 174-191), shorter versions of core were also engineered onto the polypeptide. As described in detail herein, the truncation of core to amino acid 121 yielded higher expression than the amino acid 173 truncation when engineered onto the C-terminus of the mutant NS polypeptide. The combination of most of the non-structural region fused to a C-terminally truncated core into a polypeptide is novel and has advantages for vaccine immunization. Moreover, because the aim is not necessarily to generate antibody responses to this polypeptide, there is no need to maintain a native conformation, enabling a more facile purification protocol.

Mutant HCV Non-Structural Polypeptides

Genomes of HCV strains contain a single open reading frame of approximately 9,000 to 12,000 nucleotides, which is transcribed into a polyprotein. An HCV polyprotein is cleaved to produce at least ten distinct products, in the order of NH₂-Core-E1-E2-p7-NS2-NS3-NS4a-NS4b-NS5a-NS5b-COOH. Mutant HCV polypeptides of the invention contain an N-terminal deletion in NS3, which removes or disables the catalytic domain. Preferably, the polypeptides also include the remainder of the non-structural region, although in certain embodiments, the polypeptides may include less than all of the remaining NS polypeptides, for example mutant NS polypeptides including any combinations of NS2-NS3-NS4a-NS4b-NS5a-NS5b (*e.g.*, NS3NS3-NS5a-NS5b; NS3-NS4a-NS4b; NS3-NS4a-NS4b-NS5a; NS3-NS4b-NS5a-NS5b; NS3-NS4a-NS5a; NS3-NS4b-NS5a; NS3-NS4b-NS5b; etc.).

The HCV NS3 protein functions as a protease and a helicase and occurs at approximately amino acid 1027 to amino acid 1657 of the polyprotein (numbered relative to HCV-1). *See Choo et al.* (1991) *Proc. Natl. Acad. Sci. USA* 88:2451-2455. HCV NS4 occurs at approximately amino acid 1658 to amino acid 1972, NS5a occurs at approximately amino acid 1973 to amino acid 2420, and HCV NS5b occurs at approximately amino acid 2421 to amino acid 3011 of the polyprotein (numbered relative to HCV-1) (*Choo et al.*, 1991).

The mutant polypeptides described herein can either be full-length polypeptides or portions of NS3, NS4 (NS4a and NS4b), NS5a, and NS5b polypeptides. Epitopes of NS3, NS4 (NS4a and NS4b), NS5a, NS5b, NS3NS4NS5a, and NS3NS4NS5aNS5b can

be identified by several methods. For example, NS3, NS4, NS5a, NS5b polypeptides or fusion proteins comprising any combination of the above, can be isolated, for example, by immunoaffinity purification using a monoclonal antibody for the polypeptide or protein. The isolated protein sequence can then be screened by
5 preparing a series of short peptides by proteolytic cleavage of the purified protein, which together span the entire protein sequence. By starting with, for example, 100-mer polypeptides, each polypeptide can be tested for the presence of epitopes recognized by a T cell receptor on an HCV-activated T cell, progressively smaller and overlapping fragments can then be tested from an identified 100-mer to map the epitope
10 of interest.

Epitopes recognized by a T cell receptor on an HCV-activated T cell can be identified by, for example, ⁵¹Cr release assay (see Example 2) or by lymphoproliferation assay (see Example 4). In a ⁵¹Cr release assay, target cells can be constructed that display the epitope of interest by cloning a polynucleotide encoding the
15 epitope into an expression vector and transforming the expression vector into the target cells. Non-structural polypeptides can occur in any order in the fusion protein. If desired, at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more of one or more of the polypeptides may occur in the fusion protein. Multiple viral strains of HCV occur, and NS3, NS4, NS5a, and NS5b polypeptides of any of these strains can be used in a fusion protein.

20 Nucleic acid and amino acid sequences of a number of HCV strains and isolates, including nucleic acid and amino acid sequences of NS3, NS4, NS5a, NS5b genes and polypeptides have been determined. For example, isolate HCV J1.1 is described in Kubo *et al.* (1989) Japan. Nucl. Acids Res. 17:10367-10372; Takeuchi *et al.* (1990) Gene 91:287-291; Takeuchi *et al.* (1990) J. Gen. Virol. 71:3027-3033; and
25 Takeuchi *et al.* (1990) Nucl. Acids Res. 18:4626. The complete coding sequences of two independent isolates, HCV-J and BK, are described by Kato *et al.*, (1990) Proc. Natl. Acad. Sci. USA 87:9524-9528 and Takamizawa *et al.*, (1991) J. Virol. 65:1105-1113 respectively.

Publications that describe HCV-1 isolates include Choo *et al.* (1990) Brit. Med. Bull. 46:423-441; Choo *et al.* (1991) Proc. Natl. Acad. Sci. USA 88:2451-2455 and
30 Han *et al.* (1991) Proc. Natl. Acad. Sci. USA 88:1711-1715. HCV isolates HC-J1 and HC-J4 are described in Okamoto *et al.* (1991) Japan J. Exp. Med. 60:167-177. HCV

isolates HCT 18-, HCT 23, Th, HCT 27, EC1 and EC10 are described in Weiner *et al.* (1991) *Virology* 180:842-848. HCV isolates Pt-1, HCV-K1 and HCV-K2 are described in Enomoto *et al.* (1990) *Biochem. Biophys. Res. Commun.* 170:1021-1025. HCV isolates A, C, D & E are described in Tsukiyama-Kohara *et al.* (1991) *Virus Genes* 5:243-254.

Each of the mutant HCV polypeptides containing at least portions of NS3, NS4 and NS5 can be obtained from the same HCV strain or isolate or from different HCV strains or isolates. Thus, each non-structural region of the polypeptide can be from the same HCV strain or isolate or from each different HCV strains or isolates. In addition to the mutant HCV non-structural polypeptides described herein, the proteins can contain other polypeptides derived from the HCV polyprotein. For example, it may be desirable to include polypeptides derived from the core region of the HCV polyprotein. This region occurs at amino acid positions 1-191 of the HCV polyprotein, numbered relative to HCV-1. Either the full-length protein or epitopes of the full-length protein may be used in the subject fusions, such as those epitopes found between amino acids 10-53, amino acids 10-45, amino acids 67-88, amino acids 120-130, or any of the core epitopes identified in, e.g., Houghton *et al.*, U.S. Patent No. 5,350,671; Chien *et al.*, *Proc. Natl. Acad. Sci. USA* (1992) 89:10011-10015; Chien *et al.*, *J. Gastroent. Hepatol.* (1993) 8:S33-39; Chien *et al.*, International Publication No. WO 93/00365; Chien, D.Y., International Publication No. WO 94/01778; and commonly owned, U.S. Patent No. 6,150,087. When present, additional non-structural HCV polypeptides such as core can be obtained from the same HCV strain or isolate or from different HCV strains or isolates.

Preferably, the above-described mutant proteins, as well as the individual components of these proteins, are produced recombinantly. A polynucleotide encoding these proteins can be introduced into an expression vector which can be expressed in a suitable expression system. A variety of bacterial, yeast, mammalian, insect and plant expression systems are available in the art and any such expression system can be used. Optionally, a polynucleotide encoding these proteins can be translated in a cell-free translation system. Such methods are well known in the art. The proteins also can be constructed by solid phase protein synthesis.

If desired, the mutant polypeptides, or the individual components of these polypeptides, also can contain other amino acid sequences, such as amino acid linkers or signal sequences, as well as ligands useful in protein purification, such as glutathione-S-transferase and staphylococcal protein A.

5

Polynucleotides

The polynucleotides of the present invention are not necessarily physically derived from the nucleotide sequences shown, but can be generated in any manner, including, for example, chemical synthesis or DNA replication or reverse transcription or transcription. In addition, combinations of regions corresponding to that of the designated sequences can be modified in ways known to the art to be consistent with an intended use.

The DNA encoding the desired polypeptide, whether in fused or mature form, and whether or not containing a signal sequence to permit secretion, can be ligated into expression vectors suitable for any convenient host. Both eukaryotic and prokaryotic host systems are presently used in forming recombinant polypeptides, and a summary of some of the more common control systems and host cell is given below. The polypeptide produced in such host cells is then isolated from lysed cells or from the culture medium and purified to the extent needed for its intended use.

Purification can be by techniques known in the art, for example, differential extraction, salt fractionation, chromatography on ion exchange resins, affinity chromatography, centrifugation, alkali resolubilization of insoluble protein, and the like. See, for example, Methods in Enzymology for a variety of methods for purifying proteins.

Polynucleotides contain less than an entire HCV genome and can be RNA or single- or double-stranded DNA. Preferably, the polynucleotides are isolated free of other components, such as proteins and lipids. Polynucleotides of the invention can also comprise other nucleotide sequences, such as sequences coding for linkers, signal sequences, or ligands useful in protein purification such as glutathione-S-transferase and staphylococcal protein A.

Polynucleotides encoding mutant HCV non-structural polypeptides can be isolated from a genomic library derived from nucleic acid sequences present in, for

example, the plasma, serum, or liver homogenate of an HCV infected individual or can be synthesized in the laboratory, for example, using an automatic synthesizer. An amplification method such as PCR can be used to amplify polynucleotides from either HCV genomic DNA or cDNA.

5 Further, while the polypeptides that are not NS3, NS4, or NS5 of HCV of the present invention can comprise a substantially complete viral domain, in many applications all that is required is that the polypeptide comprise an antigenic or immunogenic region of the virus. An antigenic region of a polypeptide is generally relatively small-typically 8 to 10 amino acids or less in length. Fragments of as few as 5
10 amino acids can characterize an antigenic region. These segments can correspond to regions of, for example, C, E1, or E2 epitopes. Accordingly, using the cDNAs of C, E1, or E2 as a basis, DNAs encoding short segments of C, E1, or E2 polypeptides can be expressed recombinantly either as fusion proteins, or as isolated polypeptides. In addition, short amino acid sequences can be conveniently obtained by chemical
15 synthesis.

 Polynucleotides encoding the polypeptides described herein can comprise coding sequences for these polypeptides which occur naturally or can be artificial sequences which do not occur in nature. These polynucleotides can be ligated to form a coding sequence for the fusion proteins using standard molecular biology techniques.
20 If desired, polynucleotides can be cloned into an expression vector and transformed into, for example, bacterial, yeast, insect, plant or mammalian cells so that the fusion proteins of the invention can be expressed in and isolated from a cell culture.

 The expression of polypeptides containing these domains in a variety of recombinant host cells, including, for example, bacteria, yeast, insect, plant and
25 vertebrate cells, give rise to important immunological reagents which can be used for diagnosis, detection, and vaccines.

 The general techniques used in extracting the genome from a virus, preparing and probing a cDNA library, sequencing clones, constructing expression vectors, transforming cells, performing immunological assays such as radioimmunoassays and
30 ELISA assays, for growing cells in culture, and the like are known in the art and laboratory manuals are available describing these techniques. However, as a general

guide, the following sets forth some sources currently available for such procedures, and for materials useful in carrying them out.

Both prokaryotic and eukaryotic host cells may be used for expression of desired coding sequences when appropriate control sequences which are compatible with the designated host are used. Among prokaryotic hosts, *E. coli* is most frequently used. Expression control sequences for prokaryotes include promoters, optionally containing operator portions, and ribosome binding sites. Transfer vectors compatible with prokaryotic hosts are commonly derived from, for example, pBR322, a plasmid containing operons conferring ampicillin and tetracycline resistance, and the various pUC vectors, which also contain sequences conferring antibiotic resistance markers. These markers may be used to obtain successful transformants by selection. Commonly used prokaryotic control sequences include the Beta-lactamase (penicillinase) and lactose promoter systems (Chang et al. (1977), *Nature* 198:1056), the tryptophan (*trp*) promoter system (Goeddel et al. (1980) *Nucleic Acid Res.* 8:4057), the lambda-derived P[L] promoter and N gene ribosome binding site (Shimatake et al. (1981) *Nature* 292:128) and the hybrid *tac* promoter (De Boer et al. (1983) *Proc. Natl. Acad. Sci. U.S.A.* 292:128) derived from sequences of the *trp* and *lac* UV5 promoters. The foregoing systems are particularly compatible with *E. coli*; if desired, other prokaryotic hosts such as strains of *Bacillus* or *Pseudomonas* may be used, with corresponding control sequences.

Eukaryotic hosts include mammalian and yeast cells in culture systems. Mammalian cell lines available as hosts for expression are known in the art and include many immortalized cell lines available from the American Type Culture Collection (ATCC), including HeLa cells, Chinese hamster ovary (CHO) cells, baby hamster kidney (BHK) cells, and a number of other cell lines. Suitable promoters for mammalian cells are also known in the art and include viral promoters such as that from Simian Virus 40 (SV40) (Fiers (1978), *Nature* 273:113), Rous sarcoma virus (RSV), adenovirus (ADV), and bovine papilloma virus (BPV). Mammalian cells may also require terminator sequences and poly A addition sequences; enhancer sequences which increase expression may also be included, and sequences which cause amplification of the gene may also be desirable. These sequences are known in the art. Vectors suitable for replication in mammalian cells may include viral replicons, or

sequences which insure integration of the appropriate sequences encoding NANBV epitopes into the host genome.

The vaccinia virus system can also be used to express foreign DNA in mammalian cells. To express heterologous genes, the foreign DNA is usually inserted
5 into the thymidine kinase gene of the vaccinia virus and then infected cells can be selected. This procedure is known in the art and further information can be found in these references (Mackett et al. J. Virol. 49: 857-864 (1984) and Chapter 7 in DNA Cloning, Vol. 2, IRL Press).

Yeast expression systems are also known to one of ordinary skill in the art. A
10 yeast promoter is any DNA sequence capable of binding yeast RNA polymerase and initiating the downstream (3') transcription of a coding sequence (*e.g.*, structural gene) into mRNA. A promoter will have a transcription initiation region which is usually placed proximal to the 5' end of the coding sequence. This transcription initiation region usually includes an RNA polymerase binding site (the "TATA Box") and a
15 transcription initiation site. A yeast promoter may also have a second domain called an upstream activator sequence (UAS), which, if present, is usually distal to the structural gene. The UAS permits regulated (inducible) expression. Constitutive expression occurs in the absence of a UAS. Regulated expression may be either positive or negative, thereby either enhancing or reducing transcription.

20 Yeast is a fermenting organism with an active metabolic pathway, therefore sequences encoding enzymes in the metabolic pathway provide particularly useful promoter sequences. Examples include alcohol dehydrogenase (ADH) (EP-A-0 284 044), enolase, glucokinase, glucose-6-phosphate isomerase, glyceraldehyde-3-phosphate-dehydrogenase (GAP or GAPDH), hexokinase, phosphofructokinase, 3-
25 phosphoglycerate mutase, and pyruvate kinase (PyK) (EPO-A-0 329 203). The yeast *PHOS* gene, encoding acid phosphatase, also provides useful promoter sequences (Myanohara *et al.* (1983) *Proc. Natl. Acad. Sci. USA* 80:1).

In addition, synthetic promoters which do not occur in nature also function as yeast promoters. For example, UAS sequences of one yeast promoter may be joined
30 with the transcription activation region of another yeast promoter, creating a synthetic hybrid promoter. Examples of such hybrid promoters include the ADH regulatory sequence linked to the GAP transcription activation region (US Patent Nos. 4,876,197

and 4,880,734). Other examples of hybrid promoters include promoters which consist of the regulatory sequences of either the *ADH2*, *GAL4*, *GAL10*, OR *PHO5* genes, combined with the transcriptional activation region of a glycolytic enzyme gene such as GAP or PyK (EP-A-0 164 556). Furthermore, a yeast promoter can include naturally
5 occurring promoters of non-yeast origin that have the ability to bind yeast RNA polymerase and initiate transcription. Examples of such promoters include, *inter alia*, (Cohen *et al.* (1980) *Proc. Natl. Acad. Sci. USA* 77:1078; Henikoff *et al.* (1981) *Nature* 283:835; Hollenberg *et al.* (1981) *Curr. Topics Microbiol. Immunol.* 96:119; Hollenberg *et al.* (1979) "The Expression of Bacterial Antibiotic Resistance Genes in
10 the Yeast *Saccharomyces cerevisiae*," in: *Plasmids of Medical, Environmental and Commercial Importance* (eds. K.N. Timmis and A. Puhler); Mercerau-Puigalon *et al.* (1980) *Gene* 11:163; Panthier *et al.* (1980) *Curr. Genet.* 2:109).

A DNA molecule may be expressed intracellularly in yeast. A promoter sequence may be directly linked with the DNA molecule, in which case the first amino
15 acid at the N-terminus of the recombinant protein will always be a methionine, which is encoded by the ATG start codon. If desired, methionine at the N-terminus may be cleaved from the protein by *in vitro* incubation with cyanogen bromide.

Fusion proteins provide an alternative for yeast expression systems, as well as in mammalian, baculovirus, and bacterial expression systems. Usually, a DNA
20 sequence encoding the N-terminal portion of an endogenous yeast protein, or other stable protein, is fused to the 5' end of heterologous coding sequences. Upon expression, this construct will provide a fusion of the two amino acid sequences. For example, the yeast or human superoxide dismutase (SOD) gene, can be linked at the 5' terminus of a foreign gene and expressed in yeast. The DNA sequence at the junction
25 of the two amino acid sequences may or may not encode a cleavable site. See *e.g.*, EP-A-0 196 056. Another example is a ubiquitin fusion protein. Such a fusion protein is made with the ubiquitin region that preferably retains a site for a processing enzyme (*e.g.*, ubiquitin-specific processing protease) to cleave the ubiquitin from the foreign protein. Through this method, therefore, native foreign protein can be isolated (*e.g.*,
30 WO88/024066).

Alternatively, foreign proteins can also be secreted from the cell into the growth media by creating chimeric DNA molecules that encode a fusion protein comprised of a

leader sequence fragment that provide for secretion in yeast of the foreign protein. Preferably, there are processing sites encoded between the leader fragment and the foreign gene that can be cleaved either *in vivo* or *in vitro*. The leader sequence fragment usually encodes a signal peptide comprised of hydrophobic amino acids which direct the secretion of the protein from the cell.

DNA encoding suitable signal sequences can be derived from genes for secreted yeast proteins, such as the yeast invertase gene (EP-A-0 012 873; JPO. 62,096,086) and the A-factor gene (US patent 4,588,684). Alternatively, leaders of non-yeast origin, such as an interferon leader, exist that also provide for secretion in yeast (EP-A-0 060 057).

A preferred class of secretion leaders are those that employ a fragment of the yeast alpha-factor gene, which contains both a "pre" signal sequence, and a "pro" region. The types of alpha-factor fragments that can be employed include the full-length pre-pro alpha factor leader (about 83 amino acid residues) as well as truncated alpha-factor leaders (usually about 25 to about 50 amino acid residues) (US Patents 4,546,083 and 4,870,008; EP-A-0 324 274). Additional leaders employing an alpha-factor leader fragment that provides for secretion include hybrid alpha-factor leaders made with a presequence of a first yeast, but a pro-region from a second yeast alphafactor. (*e.g.*, see WO 89/02463.)

Usually, transcription termination sequences recognized by yeast are regulatory regions located 3' to the translation stop codon, and thus together with the promoter flank the coding sequence. These sequences direct the transcription of an mRNA which can be translated into the polypeptide encoded by the DNA. Examples of transcription terminator sequence and other yeast-recognized termination sequences, such as those coding for glycolytic enzymes.

Usually, the above described components, comprising a promoter, leader (if desired), coding sequence of interest, and transcription termination sequence, are put together into expression constructs. Expression constructs are often maintained in a replicon, such as an extrachromosomal element (*e.g.*, plasmids) capable of stable maintenance in a host, such as yeast or bacteria. The replicon may have two replication systems, thus allowing it to be maintained, for example, in yeast for expression and in a prokaryotic host for cloning and amplification. Examples of such yeast-bacteria shuttle

- vectors include YEp24 (Botstein *et al.* (1979) *Gene* 8:17-24), pCI/1 (Brake *et al.* (1984) *Proc. Natl. Acad. Sci USA* 81:4642-4646), and YRp17 (Stinchcomb *et al.* (1982) *J. Mol. Biol.* 158:157). In addition, a replicon may be either a high or low copy number plasmid. A high copy number plasmid will generally have a copy number ranging from about 5 to about 200, and usually about 10 to about 150. A host containing a high copy number plasmid will preferably have at least about 10, and more preferably at least about 20. Enter a high or low copy number vector may be selected, depending upon the effect of the vector and the foreign protein on the host. See *e.g.*, Brake *et al.*, *supra*.
- Alternatively, the expression constructs can be integrated into the yeast genome with an integrating vector. Integrating vectors usually contain at least one sequence homologous to a yeast chromosome that allows the vector to integrate, and preferably contain two homologous sequences flanking the expression construct. Integrations appear to result from recombinations between homologous DNA in the vector and the yeast chromosome (Orr-Weaver *et al.* (1983) *Methods in Enzymol.* 101:228-245). An integrating vector may be directed to a specific locus in yeast by selecting the appropriate homologous sequence for inclusion in the vector. See Orr-Weaver *et al.*, *supra*. One or more expression construct may integrate, possibly affecting levels of recombinant protein produced (Rine *et al.* (1983) *Proc. Natl. Acad. Sci. USA* 80:6750). The chromosomal sequences included in the vector can occur either as a single segment in the vector, which results in the integration of the entire vector, or two segments homologous to adjacent segments in the chromosome and flanking the expression construct in the vector, which can result in the stable integration of only the expression construct.
- Usually, extrachromosomal and integrating expression constructs may contain selectable markers to allow for the selection of yeast strains that have been transformed. Selectable markers may include biosynthetic genes that can be expressed in the yeast host, such as *ADE2*, *HIS4*, *LEU2*, *TRP1*, and *ALG7*, and the G418 resistance gene, which confer resistance in yeast cells to tunicamycin and G418, respectively. In addition, a suitable selectable marker may also provide yeast with the ability to grow in the presence of toxic compounds, such as metal. For example, the presence of *CUP1*

allows yeast to grow in the presence of copper ions (Butt *et al.* (1987) *Microbiol. Rev.* 51:351).

Alternatively, some of the above described components can be put together into transformation vectors. Transformation vectors are usually comprised of a selectable
5 marker that is either maintained in a replicon or developed into an integrating vector, as described above.

Expression and transformation vectors, either extrachromosomal replicons or integrating vectors, have been developed for transformation into many yeasts. For example, expression vectors have been developed for, *inter alia*, the following yeasts:
10 *Candida albicans* (Kurtz, *et al.* (1986) *Mol. Cell. Biol.* 6:142), *Candida maltosa* (Kunze, *et al.* (1985) *J. Basic Microbiol.* 25:141). *Hansenula polymorpha* (Gleeson, *et al.* (1986) *J. Gen. Microbiol.* 132:3459; Roggenkamp *et al.* (1986) *Mol. Gen. Genet.* 202:302), *Kluyveromyces fragilis* (Das, *et al.* (1984) *J. Bacteriol.* 158:1165), *Kluyveromyces lactis* (De Louvencourt *et al.* (1983) *J. Bacteriol.* 154:737; Van den
15 Berg *et al.* (1990) *Bio/Technology* 8:135), *Pichia guilliermondii* (Kunze *et al.* (1985) *J. Basic Microbiol.* 25:141), *Pichia pastoris* (Cregg, *et al.* (1985) *Mol. Cell. Biol.* 5:3376; US Patent Nos. 4,837,148 and 4,929,555), *Saccharomyces cerevisiae* (Hinnen *et al.* (1978) *Proc. Natl. Acad. Sci. USA* 75:1929; Ito *et al.* (1983) *J. Bacteriol.* 153:163), *Schizosaccharomyces pombe* (Beach and Nurse (1981) *Nature* 300:706), and
20 *Yarrowia lipolytica* (Davidow, *et al.* (1985) *Curr. Genet.* 10:380471 Gaillardin, *et al.* (1985) *Curr. Genet.* 10:49).

Methods of introducing exogenous DNA into yeast hosts are well-known in the art, and usually include either the transformation of spheroplasts or of intact yeast cells treated with alkali cations. Transformation procedures usually vary with the yeast
25 species to be transformed. (See *e.g.*, Kurtz *et al.* (1986) *Mol. Cell. Biol.* 6:142; Kunze *et al.* (1985) *J. Basic Microbiol.* 25:141; *Candida*; Gleeson *et al.* (1986) *J. Gen. Microbiol.* 132:3459; Roggenkamp *et al.* (1986) *Mol. Gen. Genet.* 202:302; *Hansenula*; Das *et al.* (1984) *J. Bacteriol.* 158:1165; De Louvencourt *et al.* (1983) *J. Bacteriol.* 154:1165; Van den Berg *et al.* (1990) *Bio/Technology* 8:135;
30 *Kluyveromyces*; Cregg *et al.* (1985) *Mol. Cell. Biol.* 5:3376; Kunze *et al.* (1985) *J. Basic Microbiol.* 25:141; US Patent Nos. 4,837,148 and 4,929,555; *Pichia*; Hinnen *et al.* (1978) *Proc. Natl. Acad. Sci. USA* 75:1929; Ito *et al.* (1983) *J. Bacteriol.*

153:163 *Saccharomyces*; Beach and Nurse (1981) *Nature* 300:706;
Schizosaccharomyces; Davidow *et al.* (1985) *Curr. Genet.* 10:39; Gaillardin *et al.*
(1985) *Curr. Genet.* 10:49; Yarrowia).

Bacterial expression techniques are known in the art. A bacterial promoter is
5 any DNA sequence capable of binding bacterial RNA polymerase and initiating the
downstream (3') transcription of a coding sequence (*e.g.*, structural gene) into mRNA.
A promoter will have a transcription initiation region which is usually placed proximal
to the 5' end of the coding sequence. This transcription initiation region usually
includes an RNA polymerase binding site and a transcription initiation site. A bacterial
10 promoter may also have a second domain called an operator, that may overlap an
adjacent RNA polymerase binding site at which RNA synthesis begins. The operator
permits negative regulated (inducible) transcription, as a gene repressor protein may
bind the operator and thereby inhibit transcription of a specific gene. Constitutive
expression may occur in the absence of negative regulatory elements, such as the
15 operator. In addition, positive regulation may be achieved by a gene activator protein
binding sequence, which, if present is usually proximal (5') to the RNA polymerase
binding sequence. An example of a gene activator protein is the catabolite activator
protein (CAP), which helps initiate transcription of the lac operon in *Escherichia coli*
(*E. coli*) (Raibaud *et al.* (1984) *Annu. Rev. Genet.* 18:173). Regulated expression
20 may therefore be either positive or negative, thereby either enhancing or reducing
transcription.

Expression and transformation vectors, either extra-chromosomal replicons or
integrating vectors, have been developed for transformation into many bacteria. For
example, expression vectors have been developed for, *inter alia*, the following bacteria:
25 *Bacillus subtilis* (Palva *et al.* (1982) *Proc. Natl. Acad. Sci. USA* 79:5582; EP-A-0
036 259 and EP-A-0 063 953; WO 84/04541), *Escherichia coli* (Shimatake *et al.*
(1981) *Nature* 292:128; Amann *et al.* (1985) *Gene* 40:183; Studier *et al.* (1986) *J.*
Mol. Biol. 189:113; EP-A-0 036 776, EP-A-0 136 829 and EP-A-0 136 907),
Streptococcus cremoris (Powell *et al.* (1988) *Appl. Environ. Microbiol.* 54:655);
30 *Streptococcus lividans* (Powell *et al.* (1988) *Appl. Environ. Microbiol.* 54:655),
Streptomyces lividans (US patent 4,745,056).

Methods of introducing exogenous DNA into bacterial hosts are well-known in the art, and usually include either the transformation of bacteria treated with CaCl_2 or other agents, such as divalent cations and DMSO. DNA can also be introduced into bacterial cells by electroporation. Transformation procedures usually vary with the bacterial species to be transformed. (See *e.g.*, Masson *et al.* (1989) *FEMS Microbiol. Lett.* 60:273; Palva *et al.* (1982) *Proc. Natl. Acad. Sci. USA* 79:5582; EP-A-0 036 259 and EP-A-0 063 953; WO 84/04541, Bacillus, Miller *et al.* (1988) *Proc. Natl. Acad. Sci.* 85:856; Wang *et al.* (1990) *J. Bacteriol.* 172:949; Campylobacter, Cohen *et al.* (1973) *Proc. Natl. Acad. Sci.* 69:2110; Dower *et al.* (1988) *Nucleic Acids Res.* 16:6127; Kushner (1978) "An improved method for transformation of *Escherichia coli* with ColE1-derived plasmids. In *Genetic Engineering: Proceedings of the International Symposium on Genetic Engineering* (eds. H.W. Boyer and S. Nicosia); Mandel *et al.* (1970) *J. Mol. Biol.* 53:159; Taketo (1988) *Biochim. Biophys. Acta* 949:318; *Escherichia*; Chassy *et al.* (1987) *FEMS Microbiol. Lett.* 44:173 Lactobacillus; Fiedler *et al.* (1988) *Anal. Biochem* 170:38, *Pseudomonas*; Augustin *et al.* (1990) *FEMS Microbiol. Lett.* 66:203, *Staphylococcus*, Barany *et al.* (1980) *J. Bacteriol.* 144:698; Harlander (1987) "Transformation of *Streptococcus lactis* by electroporation, in: *Streptococcal Genetics* (ed. J. Ferretti and R. Curtiss III); Perry *et al.* (1981) *Infect. Immun.* 32:1295; Powell *et al.* (1988) *Appl. Environ. Microbiol.* 54:655; Somkuti *et al.* (1987) *Proc. 4th Evr. Cong. Biotechnology* 1:412, *Streptococcus*).

In addition, viral antigens can be expressed in insect cells by the Baculovirus system. A general guide to Baculovirus expression by Summer and Smith is *A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures* (Texas Agricultural Experiment Station Bulletin No. 1555). To incorporate the heterologous gene into the Baculovirus genome the gene is first cloned into a transfer vector containing some Baculovirus sequences. This transfer vector, when it is cotransfected with wild-type virus into insect cells, will recombine with the wild-type virus. Usually, the transfer vector will be engineered so that the heterologous gene will disrupt the wild-type Baculovirus polyhedron gene. This disruption enables easy selection of the recombinant virus since the cells infected with the recombinant virus will appear phenotypically different from the cells infected with the wild-type virus. The purified

recombinant virus can be used to infect cells to express the heterologous gene. The foreign protein can be secreted into the medium if a signal peptide is linked in frame to the heterologous gene; otherwise, the protein will be bound in the cell lysates. For further information, see Smith et al *Mol. & Cell. Biol.* 3:2156-2165 (1983) or Luckow and Summers in *Virology* 17: 31-39 (1989).

Baculovirus expression can also be affected in plant cells. There are many plant cell culture and whole plant genetic expression systems known in the art. Exemplary plant cellular genetic expression systems include those described in patents, such as: US 5,693,506; US 5,659,122; and US 5,608,143. Additional examples of genetic expression in plant cell culture has been described by Zenk, *Phytochemistry* 30:3861-3863 (1991). Descriptions of plant protein signal peptides may be found in addition to the references described above in Vaulcombe et al., *Mol. Gen. Genet.* 209:33-40 (1987); Chandler et al., *Plant Molecular Biology* 3:407-418 (1984); Rogers, *J. Biol. Chem.* 260:3731-3738 (1985); Rothstein et al., *Gene* 55:353-356 (1987); Whittier et al., *Nucleic Acids Research* 15:2515-2535 (1987); Wirsal et al., *Molecular Microbiology* 3:3-14 (1989); Yu et al., *Gene* 122:247-253 (1992). A description of the regulation of plant gene expression by the phytohormone, gibberellic acid and secreted enzymes induced by gibberellic acid can be found in R.L. Jones and J. MacMillin, *Gibberellins*: in: *Advanced Plant Physiology*, Malcolm B. Wilkins, ed., 1984 Pitman Publishing Limited, London, pp. 21-52. References that describe other metabolically-regulated genes: Sheen, *Plant Cell*, 2:1027-1038(1990); Maas et al., *EMBO J.* 9:3447-3452 (1990); Benkel and Hickey, *Proc. Natl. Acad. Sci.* 84:1337-1339 (1987).

All plants from which protoplasts can be isolated and cultured to give whole regenerated plants can be transformed by the present invention so that whole plants are recovered which contain the transferred gene. It is known that practically all plants can be regenerated from cultured cells or tissues, including but not limited to all major species of sugarcane, sugar beet, cotton, fruit and other trees, legumes and vegetables. Some suitable plants include, for example, species from the genera *Fragaria*, *Lotus*, *Medicago*, *Onobrychis*, *Trifolium*, *Trigonella*, *Vigna*, *Citrus*, *Linum*, *Geranium*, *Manihot*, *Daucus*, *Arabidopsis*, *Brassica*, *Raphanus*, *Sinapis*, *Atropa*, *Capsicum*, *Datura*, *Hyoscyamus*, *Lycopersion*, *Nicotiana*, *Solanum*, *Petunia*, *Digitalis*, *Majorana*, *Cichorium*, *Helianthus*, *Lactuca*, *Bromus*, *Asparagus*, *Antirrhinum*, *Hererocallis*,

Nemesia, Pelargonium, Panicum, Pennisetum, Ranunculus, Senecio, Salpiglossis, Cucumis, Browaalia, Glycine, Lolium, Zea, Triticum, Sorghum, and Datura.

Transformation can be by any method for introducing polynucleotides into a host cell, including, for example packaging the polynucleotide in a virus and
5 transducing a host cell with the virus, and by direct uptake of the polynucleotide. The transformation procedure used depends upon the host to be transformed. Bacterial transformation by direct uptake generally employs treatment with calcium or rubidium chloride (Cohen (1972), Proc. Natl. Acad. Sci. U.S.A. 69:2110; Maniatis et al. (1982), MOLECULAR CLONING; A LABORATORY MANUAL (Cold Spring Harbor Press,
10 Cold Spring Harbor, N.Y.). Yeast transformation by direct uptake may be carried out using the method of Hinnen et al. (1978) Proc. Natl. Acad. Sci. U.S.A. 75: 1929. Mammalian transformations by direct uptake may be conducted using the calcium phosphate precipitation method of Graham and Van der Eb (1978), Virology 52:546 or the various known modifications thereof.

15 Vector construction employs techniques which are known in the art. Site-specific DNA cleavage is performed by treating with suitable restriction enzymes under conditions which generally are specified by the manufacturer of these commercially available enzymes. The cleaved fragments may be separated using polyacrylamide or agarose gel electrophoresis techniques, according to the general procedures found in
20 Methods in Enzymology (1980) 65:499-560. Sticky ended cleavage fragments may be blunt ended using E. coli DNA polymerase I (Klenow) in the presence of the appropriate deoxynucleotide triphosphates (dNTPs) present in the mixture. Treatment with S1 nuclease may also be used, resulting in the hydrolysis of any single stranded DNA portions.

25 Ligations are carried out using standard buffer and temperature conditions using T4 DNA ligase and ATP; sticky end ligations require less ATP and less ligase than blunt end ligations. When vector fragments are used as part of a ligation mixture, the vector fragment is often treated with bacterial alkaline phosphatase (BAP) or calf intestinal alkaline phosphatase to remove the 5'-phosphate and thus prevent religation
30 of the vector; alternatively, restriction enzyme digestion of unwanted fragments can be used to prevent ligation. Ligation mixtures are transformed into suitable cloning hosts,

such as *E. coli*, and successful transformants selected by, for example, antibiotic resistance, and screened for the correct construction.

Synthetic oligonucleotides may be prepared using an automated oligonucleotide synthesizer as described by Warner (1984), DNA 3:401. If desired, the synthetic strands
5 may be labeled with ^{32}P by treatment with polynucleotide kinase in the presence of ^{32}P -ATP, using standard conditions for the reaction. DNA sequences, including those isolated from cDNA libraries, may be modified by known techniques, including, for example site directed mutagenesis, as described by Zoller (1982), Nucleic Acids Res. 10:6487.

10 The expression constructs of the present invention, including the desired fusion, or individual expression constructs comprising the individual components of these fusions, may be used for nucleic acid immunization, to activate HCV-specific T cells, using standard gene delivery protocols. Methods for gene delivery are known in the art. See, e.g., U.S. Patent Nos. 5,399,346, 5,580,859, 5,589,466. Genes can be
15 delivered either directly to the vertebrate subject or, alternatively, delivered *ex vivo*, to cells derived from the subject and the cells reimplanted in the subject. For example, the constructs can be delivered as plasmid DNA, e.g., contained within a plasmid, such as pBR322, pUC, or ColE1

Additionally, the expression constructs can be packaged in liposomes prior to
20 delivery to the cells. Lipid encapsulation is generally accomplished using liposomes which are able to stably bind or entrap and retain nucleic acid. The ratio of condensed DNA to lipid preparation can vary but will generally be around 1:1 (mg DNA:micromoles lipid), or more of lipid. For a review of the use of liposomes as carriers for delivery of nucleic acids, see, Hug and Sleight, *Biochim. Biophys. Acta*.
25 (1991) 1097:1-17; Straubinger et al., in *Methods of Enzymology* (1983), Vol. 101, pp. 512-527.

Liposomal preparations for use with the present invention include cationic (positively charged), anionic (negatively charged) and neutral preparations, with cationic liposomes particularly preferred. Cationic liposomes are readily available. For
30 example, N[1-2,3-dioleoyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, NY. (See, also, Felgner et al., *Proc. Natl. Acad. Sci. USA* (1987) 84:7413-7416). Other

commercially available lipids include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer). Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g., Szoka et al., *Proc. Natl. Acad. Sci. USA* (1978) 75:4194-4198; PCT Publication No. WO 90/11092 for a
5 description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. The various liposome-nucleic acid complexes are prepared using methods known in the art. See, e.g., Straubinger et al., in *METHODS OF IMMUNOLOGY* (1983), Vol. 101, pp. 512-527; Szoka et al., *Proc. Natl. Acad. Sci. USA* (1978) 75:4194-4198; Papahadjopoulos et al., *Biochim. Biophys. Acta* (1975) 394:483; Wilson et al., *Cell* (1979) 17:77; Deamer and Bangham, *Biochim. Biophys. Acta* (1976) 443:629; Ostro et al., *Biochem. Biophys. Res. Commun.* (1977) 76:836; Fraley et al., *Proc. Natl. Acad. Sci. USA* (1979) 76:3348; Enoch and Strittmatter, *Proc. Natl. Acad. Sci. USA* (1979) 76:145; Fraley et al., *J. Biol. Chem.* (1980) 255:10431; Szoka and Papahadjopoulos, *Proc. Natl. Acad. Sci. USA* (1978) 75:145; and Schaefer-Ridder et al., *Science* (1982) 215:166.
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15

The DNA can also be delivered in cochleate lipid compositions similar to those described by Papahadjopoulos et al., *Biochem. Biophys. Acta.* (1975) 394:483-491. See, also, U.S. Patent Nos. 4,663,161 and 4,871,488.

A number of viral based systems have been developed for gene transfer into
20 mammalian cells. For example, retroviruses provide a convenient platform for gene delivery systems, such as murine sarcoma virus, mouse mammary tumor virus, Moloney murine leukemia virus, and Rous sarcoma virus. A selected gene can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to cells of the subject
25 either *in vivo* or *ex vivo*. A number of retroviral systems have been described (U.S. Patent No. 5,219,740; Miller and Rosman, *BioTechniques* (1989) 7:980-990; Miller, A.D., *Human Gene Therapy* (1990) 1:5-14; Scarpa et al., *Virology* (1991) 180:849-852; Burns et al., *Proc. Natl. Acad. Sci. USA* (1993) 90:8033-8037; and Boris-Lawrie and Temin, *Cur. Opin. Genet. Develop.* (1993) 3:102-109. Briefly, retroviral gene delivery
30 vehicles of the present invention may be readily constructed from a wide variety of retroviruses, including for example, B, C, and D type retroviruses as well as spumaviruses and lentiviruses such as FIV, HIV, HIV-1, HIV-2 and SIV (see RNA

Tumor Viruses, Second Edition, Cold Spring Harbor Laboratory, 1985). Such retroviruses may be readily obtained from depositories or collections such as the American Type Culture Collection ("ATCC"; 10801 University Blvd., Manassas, VA 20110-2209), or isolated from known sources using commonly available techniques.

5 A number of adenovirus vectors have also been described, such as adenovirus Type 2 and Type 5 vectors. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham, *J. Virol.* (1986) 57:267-274; Bett et al., *J. Virol.* (1993) 67:5911-5921; Mittereder et al., *Human Gene Therapy* (1994) 5:717-729; Seth et al., *J. Virol.* (1994) 68:933-940; Barr et al., *Gene Therapy* (1994) 1:51-58; Berkner, K.L. *BioTechniques* (1988) 6:616-629; and Rich et al., *Human Gene Therapy* (1993) 4:461-476).

 Molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al., *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et al., *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery.

15 Members of the Alphavirus genus, such as but not limited to vectors derived from the Sindbis and Semliki Forest viruses, VEE, will also find use as viral vectors for delivering the gene of interest. For a description of Sindbis-virus derived vectors useful for the practice of the instant methods, see, Dubensky et al., *J. Virol.* (1996) 70:508-519; and International Publication Nos. WO 95/07995 and WO 96/17072.

20 Other vectors can be used, including but not limited to simian virus 40, cytomegalovirus. Bacterial vectors, such as Salmonella ssp. *Yersinia enterocolitica*, *Shigella* spp., *Vibrio cholerae*, Mycobacterium strain BCG, and *Listeria monocytogenes* can be used. Minichromosomes such as MC and MC1, bacteriophages, cosmids (plasmids into which phage lambda *cos* sites have been inserted) and replicons (genetic elements that are capable of replication under their own control in a cell) can also be used.

25 The expression constructs may also be encapsulated, adsorbed to, or associated with, particulate carriers. Such carriers present multiple copies of a selected molecule to the immune system and promote trapping and retention of molecules in local lymph nodes. The particles can be phagocytosed by macrophages and can enhance antigen presentation through cytokine release. Examples of particulate carriers include those

derived from polymethyl methacrylate polymers, as well as microparticles derived from poly(lactides) and poly(lactide-co-glycolides), known as PLG. See, e.g., Jeffery et al., *Pharm. Res.* (1993) 10:362-368; and McGee et al., *J. Microencap.* (1996).

A wide variety of other methods can be used to deliver the expression
5 constructs to cells. Such methods include DEAE dextran-mediated transfection, calcium phosphate precipitation, polylysine- or polyornithine-mediated transfection, or precipitation using other insoluble inorganic salts, such as strontium phosphate, aluminum silicates including bentonite and kaolin, chromic oxide, magnesium silicate, talc, and the like. Other useful methods of transfection include electroporation,
10 sonoporation, protoplast fusion, liposomes, peptoid delivery, or microinjection. See, e.g., Sambrook et al., *supra*, for a discussion of techniques for transforming cells of interest; and Felgner, P.L., *Advanced Drug Delivery Reviews* (1990) 5:163-187, for a review of delivery systems useful for gene transfer. One particularly effective method of delivering DNA using electroporation is described in International Publication No.
15 WO/0045823.

Additionally, biolistic delivery systems employing particulate carriers such as gold and tungsten, are especially useful for delivering the expression constructs of the present invention. The particles are coated with the construct to be delivered and accelerated to high velocity, generally under a reduced atmosphere, using a gun powder
20 discharge from a "gene gun." For a description of such techniques, and apparatuses useful therefore, see, e.g., U.S. Patent Nos. 4,945,050; 5,036,006; 5,100,792; 5,179,022; 5,371,015; and 5,478,744.

Compositions

25 The invention also provides compositions comprising the HCV polypeptides or polynucleotides described herein. Such compositions are useful as diagnostics, for example, using the mutant polypeptides (or polynucleotides encoding these polypeptides) in diagnostic reagents. Diagnostics using polypeptides and polynucleotides are known to those of skill in the art.

30 In addition, immunogenic compounds can be prepared from one or more immunogenic polypeptides derived from the polypeptides described herein, for example the Δ NS35 polypeptide. The preparation of immunogenic compounds which

contain immunogenic polypeptide(s) as active ingredients is known to one skilled in the art. Typically, such immunogenic compounds are prepared as injectables; either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection can also be prepared. The preparation can also be emulsified, or
5 the protein encapsulated in liposomes.

Immunogenic and diagnostic compositions of the invention preferably comprise a pharmaceutically acceptable carrier. The carrier should not itself induce the production of antibodies harmful to the host. Pharmaceutically acceptable carriers are well known to those in the art. Such carriers include, but are not limited to, large,
10 slowly metabolized, macromolecules, such as proteins, polysaccharides such as latex functionalized sepharose, agarose, cellulose, cellulose beads and the like, polylactic acids, polyglycolic acids, polymeric amino acids such as polyglutamic acid, polylysine, and the like, amino acid copolymers, and inactive virus particles.

Pharmaceutically acceptable salts can also be used in compositions of the invention, for example, mineral salts such as hydrochlorides, hydrobromides,
15 phosphates, or sulfates, as well as salts of organic acids such as acetates, propionates, malonates, or benzoates. Especially useful protein substrates are serum albumins, keyhole limpet hemocyanin, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid, and other proteins well known to those of skill in the art. Compositions
20 of the invention can also contain liquids or excipients, such as water, saline, glycerol, dextrose, ethanol, or the like, singly or in combination, as well as substances such as wetting agents, emulsifying agents, or pH buffering agents. Liposomes can also be used as a carrier for a composition of the invention, such liposomes are described above.

25 If desired, co-stimulatory molecules which improve immunogen presentation to lymphocytes, such as B7-1 or B7-2, or cytokines such as GM-CSF, IL-2, and IL-12, can be included in a composition of the invention. Optionally, adjuvants can also be included in a composition. Adjuvants which can be used include, but are not limited to:
(1) aluminum salts (alum), such as aluminum hydroxide, aluminum phosphate,
30 aluminum sulfate, etc; (2) oil-in-water emulsion formulations (with or without other specific immunostimulating agents such as muramyl peptides (see below) or bacterial cell wall components), such as for example (a) MF59 (PCT Publ. No. WO 90/14837),

containing 5% Squalene, 0.5% Tween 80, and 0.5% Span 85 (optionally containing various amounts of MTP-PE), formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA), (b) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-blocked polymer L121, and thr-MDP (see below) either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion, and (c) RibiTM adjuvant system (RAS), (Ribi Immunochem, Hamilton, MT) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (DetoxTM); (3) saponin adjuvants, such as StimulonTM (Cambridge Bioscience, Worcester, MA) may be used or particles generated therefrom such as ISCOMs (immunostimulating complexes); (4) Complete Freund's Adjuvant (CFA) and Incomplete Freund's Adjuvant (IFA); (5) cytokines, such as interleukins (e.g., IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, *etc.*), interferons (e.g., gamma interferon), macrophage colony stimulating factor (M-CSF), tumor necrosis factor (TNF), etc; (6) detoxified mutants of a bacterial ADP-ribosylating toxin such as a cholera toxin (CT), a pertussis toxin (PT), or an E. coli heat-labile toxin (LT), particularly LT-K63, LT-R72, CT-S109, PT-K9/G129; see, e.g., WO 93/13302 and WO 92/19265; (7) other substances that act as immunostimulating agents to enhance the effectiveness of the composition; and (8) microparticles with adsorbed macromolecules, as described in copending U.S. Patent Application Serial No. 09/285,855 (filed April 2, 1999) and international Patent Application Serial No. PCT/US99/17308 (filed July 29, 1999). Alum and MF59 are preferred. The effectiveness of an adjuvant can be determined by measuring the amount of antibodies directed against an immunogenic polypeptide containing an HCV antigenic sequence resulting from administration of this polypeptide in immunogenic compounds which are also comprised of the various adjuvants.

As mentioned above, muramyl peptides include, but are not limited to, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), -acetyl-normuramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to nor-MDP), N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine (CGP 19835A, referred to as MTP-PE), *etc.*

Thus, such recombinant or synthetic HCV polypeptides can be used in vaccines and as diagnostics. Further, antibodies raised against these polypeptides can also be used as diagnostics, or for passive immunotherapy. In addition, antibodies to these polypeptides are useful for isolating and identifying HCV particles.

- 5 Native HCV antigens can also be isolated from HCV virions. The virions can be grown in HCV infected cells in tissue culture, or in an infected host.

Administration and Delivery

- 10 The polynucleotide and polypeptide compositions described herein (*e.g.*, immunogenic compounds) may be administered to a subject using any suitable delivery means. Methods of delivering nucleic acids into host cells are discussed above. Further, HCV polynucleotides and/or polypeptides can be administered parenterally, by injection, usually, subcutaneously, intramuscularly, transdermally or transcutaneously. Certain adjuvants, *e.g.* LTK63, LTR72 or PLG formulations, can be administered
- 15 intranasally or orally. Additional formulations which are suitable for other modes of administration include suppositories. For suppositories, traditional binders and carriers can include, for example, polyalkylene glycols or triglycerides; such suppositories can be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Other oral formulations include such normally employed excipients
- 20 as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

- 25 The polypeptides of the present invention can be formulated into the immunogenic compound as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the
- 30 like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric

hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

The immunogenic compounds are administered in a manner compatible with the dosage formulation, and in such amount as will be prophylactically and/or
5 therapeutically effective. The quantity to be administered, which is generally in the range of 5 micrograms to 250 micrograms of polypeptide per dose, depends on the subject to be treated, capacity of the subject's immune system to synthesize antibodies, and the degree of protection desired. Precise amounts of active ingredient required to be administered may depend on the judgment of the practitioner and can be peculiar to
10 each subject.

The immunogenic compound can be given in a single dose schedule, or preferably in a multiple dose schedule. A multiple dose schedule is one in which a primary course of vaccination can be with 1-10 separate doses, followed by other doses given at subsequent time intervals required to maintain and or reenforce the immune
15 response, for example, at 1-4 months for a second dose, and if needed, a subsequent dose(s) after several months. Further, the course of administration may include polynucleotides and polypeptides, together or sequentially (for example, priming with a polynucleotide composition and boosting with a polypeptide composition). The dosage regimen will also, at least in part, be determined by the need of the individual and be
20 dependent upon the judgment of the practitioner.

In certain embodiments, administration of the polynucleotides and polypeptides described herein is used to activate T cells. In addition to the practical advantages of simplicity of construction and modification, administration of polynucleotides encoding mutant NS polypeptides results in the synthesis of a mutant NS polypeptide in the host.
25 Thus, these immunogens are presented to the host immune system with native post-translational modifications, structure, and conformation. The polynucleotides are preferably injected intramuscularly to a large mammal, such as a human, at a dose of 0.5, 0.75, 1.0, 1.5, 2.0, 2.5, 5 or 10 mg/kg.

The proteins and/or polynucleotides can be administered either to a mammal
30 which is not infected with an HCV or can be administered to an HCV-infected mammal. The particular dosages of the polynucleotides or fusion proteins in a composition or will depend on many factors including, but not limited to the species,

age, and general condition of the mammal to which the composition is administered, and the mode of administration of the composition. An effective amount of the composition of the invention can be readily determined using only routine experimentation. *In vitro* and *in vivo* models can be employed to identify appropriate
5 doses. Generally, 0.5, 0.75, 1.0, 1.5, 2.0, 2.5, 5 or 10 mg will be administered to a large mammal, such as a baboon, chimpanzee, or human. If desired, co-stimulatory molecules or adjuvants can also be provided before, after, or together with the compositions.

10 **Antibodies and Diagnostics**

Antibodies, both monoclonal and polyclonal, which are directed against HCV epitopes are particularly useful in diagnosis, and those which are neutralizing are useful in passive immunotherapy. Monoclonal antibodies, in particular, may be used to raise anti-idiotypic antibodies.

15 Anti-idiotypic antibodies are immunoglobulins which carry an "internal image" of the antigen of the infectious agent against which protection is desired. Techniques for raising anti-idiotypic antibodies are known in the art. See, e.g., Grzych (1985), Nature 316:74; MacNamara et al. (1984), Science 226:1325, Uytdehaag et al (1985), J. Immunol. 134:1225. These anti-idiotypic antibodies may also be useful for treatment
20 and/or diagnosis of NANBH, as well as for an elucidation of the immunogenic regions of HCV antigens.

 An immunoassay for viral antigen may use, for example, a monoclonal antibody directed towards a viral epitope, a combination of monoclonal antibodies directed towards epitopes of one viral polypeptide, monoclonal antibodies directed towards
25 epitopes of different viral polypeptides, polyclonal antibodies directed towards the same viral antigen, polyclonal antibodies directed towards different viral antigens or a combination of monoclonal and polyclonal antibodies.

 Immunoassay protocols may be based, for example, upon competition, or direct reaction, or sandwich type assays. Protocols may also, for example, use solid supports,
30 or may be by immunoprecipitation. Most assays involve the use of labeled antibody or polypeptide. The labels may be, for example, fluorescent, chemiluminescent, radioactive, or dye molecules. Assays which amplify the signals from the probe are also

known. Examples of which are assays which utilize biotin and avidin, and enzyme-labeled and mediated immunoassays, such as ELISA assays.

An enzyme-linked immunosorbent assay (ELISA) can be used to measure either antigen or antibody concentrations. This method depends upon conjugation of an
5 enzyme to either an antigen or an antibody, and uses the bound enzyme activity as a quantitative label. To measure antibody, the known antigen is fixed to a solid phase (e.g., a microplate or plastic cup), incubated with test serum dilutions, washed, incubated with anti-immunoglobulin labeled with an enzyme, and washed again. Enzymes suitable for labeling are known in the art, and include, for example,
10 horseradish peroxidase. Enzyme activity bound to the solid phase is measured by adding the specific substrate, and determining product formation or substrate utilization colorimetrically. The enzyme activity bound is a direct function of the amount of antibody bound.

To measure antigen, a known specific antibody is fixed to the solid phase, the
15 test material containing antigen is added, after an incubation the solid phase is washed, and a second enzyme-labeled antibody is added. After washing, substrate is added, and enzyme activity is estimated colorimetrically, and related to antigen concentration.

The HCV fusion proteins, such as NS3 mutant and core fusion proteins, can also be used to produce HCV-specific polyclonal and monoclonal antibodies. HCV-
20 specific polyclonal and monoclonal antibodies specifically bind to HCV antigens.

Polyclonal antibodies can be produced by administering the fusion protein to a mammal, such as a mouse, a rabbit, a goat, or a horse. Serum from the immunized animal is collected and the antibodies are purified from the plasma by, for example, precipitation with ammonium sulfate, followed by chromatography, preferably affinity
25 chromatography. Techniques for producing and processing polyclonal antisera are known in the art.

Monoclonal antibodies directed against HCV-specific epitopes present in the fusion proteins can also be readily produced. Normal B cells from a mammal, such as a mouse, immunized with, e.g., a mutant NS3 polypeptide or NS-core fusion protein can
30 be fused with, for example, HAT-sensitive mouse myeloma cells to produce hybridomas. Hybridomas producing HCV-specific antibodies can be identified using

RIA or ELISA and isolated by cloning in semi-solid agar or by limiting dilution.

Clones producing HCV-specific antibodies are isolated by another round of screening.

Antibodies, either monoclonal and polyclonal, which are directed against HCV epitopes, are particularly useful for detecting the presence of HCV or HCV antigens in a sample, such as a serum sample from an HCV-infected human. An immunoassay for an HCV antigen may utilize one antibody or several antibodies. An immunoassay for an HCV antigen may use, for example, a monoclonal antibody directed towards an HCV epitope, a combination of monoclonal antibodies directed towards epitopes of one HCV polypeptide, monoclonal antibodies directed towards epitopes of different HCV polypeptides, polyclonal antibodies directed towards the same HCV antigen, polyclonal antibodies directed towards different HCV antigens, or a combination of monoclonal and polyclonal antibodies. Immunoassay protocols may be based, for example, upon competition, direct reaction, or sandwich type assays using, for example, labeled antibody. The labels may be, for example, fluorescent, chemiluminescent, or radioactive.

The polyclonal or monoclonal antibodies may further be used to isolate HCV particles or antigens by immunoaffinity columns. The antibodies can be affixed to a solid support by, for example, adsorption or by covalent linkage so that the antibodies retain their immunoselective activity. Optionally, spacer groups may be included so that the antigen binding site of the antibody remains accessible. The immobilized antibodies can then be used to bind HCV particles or antigens from a biological sample, such as blood or plasma. The bound HCV particles or antigens are recovered from the column matrix by, for example, a change in pH.

25 **Methods of Eliciting Immune Responses**

HCV-specific T cells that are activated by the above-described polypeptides, expressed *in vivo* or *in vitro* preferably recognize an epitope of an HCV polypeptide such as a mutant NS3 polypeptide, including an epitope of a mutant HCV polypeptide. HCV-specific T cells can be CD8⁺ or CD4⁺.

30 HCV-specific CD8⁺ T cells preferably are cytotoxic T lymphocytes (CTL) which can kill HCV-infected cells that display NS3, NS4, NS5a, NS5b epitopes complexed with an MHC class I molecule. HCV-specific CD8⁺ T cells may also

express interferon- γ (IFN- γ). HCV-specific CD8⁺ T cells can be detected by, for example, ⁵¹Cr release assays. ⁵¹Cr release assays measure the ability of HCV-specific CD8⁺ T cells to lyse target cells displaying an nonstructural (e.g., mutant NS) epitope. HCV-specific CD8⁺ T cells which express IFN- γ can also be detected by

5 immunological methods, preferably by intracellular staining for IFN- γ after *in vitro* stimulation with a mutant NS polypeptide.

HCV-specific CD4⁺ cells activated by the above-described polypeptides, expressed *in vivo* or *in vitro*, and combinations of the individual components of these proteins, preferably recognize an epitope of a mutant non-structural polypeptide, including an epitope of a mutant protein, that is bound to an MHC class II molecule on an HCV-infected cell and proliferate in response to stimulating mutant peptides.

HCV-specific CD4⁺ T cells can be detected by a lymphoproliferation assay. Lymphoproliferation assays measure the ability of HCV-specific CD4⁺ T cells to proliferate in response to an epitope.

15 Mutant NS (or fusions thereof with core, envelope or other viral polypeptides) can be used to activate HCV-specific T cells either *in vitro* or *in vivo*. Activation of HCV-specific T cells can be used, *inter alia*, to provide model systems to optimize CTL responses to HCV and to provide prophylactic or therapeutic treatment against HCV infection. For *in vitro* activation, proteins are preferably supplied to T cells via a plasmid or a viral vector, such as an adenovirus vector, as described above.

Polyclonal populations of T cells can be derived from the blood, and preferably from peripheral lymphoid organs, such as lymph nodes, spleen, or thymus, of mammals that have been infected with an HCV. Preferred mammals include mice, chimpanzees, baboons, and humans. The HCV serves to expand the number of activated HCV-specific T cells in the mammal. The HCV-specific T cells derived from the mammal can then be restimulated *in vitro* by adding HCV epitopic peptides to the T cells. The HCV-specific T cells can then be tested for, *inter alia*, proliferation (e.g., lymphoproliferation assays known in the art), the production of IFN- γ , and the ability to lyse target cells displaying HCV NS epitopes *in vitro*.

30

The following examples are meant to illustrate the invention and are not meant to limit it in any way. Those of ordinary skill in the art will recognize modifications within the spirit and scope of the invention as set forth herein.

5

EXAMPLES

Example 1: Constructs

pCMV-II: pCMV-II (Figure 7, SEQ ID NO:5) was created to contain the human CMV promoter, enhancer, intron A, polylinker and the bovine growth hormone terminator in a deleted-pUC backbone (Life Technologies).

pT7-HCV: pT7-HCV was created in a polylinker-modified pUC vector to contain full-length HCV cDNA preceded by a synthetic T7 promoter. pT7-HCV also contains the complete 5' UTR and the poly A version of the 3' UTR.

pCMV.ΔNS35: To generate pCMV.ΔNS35 (Figure 5, SEQ ID NO:3), a two step procedure was undertaken. First, a PCR product was generated from pT7-HCV that corresponded to the following: a 5' EcoRI site, followed by the Kozak sequence of ACCATGG; the initiator ATG followed by amino acid #1242 and continuing to the StuI site. Second, the StuI to XbaI fragment from a full-length genomic clone was isolated. The genomic clone consisted of the T7 promoter fused to the full-length HCV cDNA with the poly A version of the 3' end, in a pUC vector. Finally, the EcoRI-StuI and StuI-XbaI fragments were ligated into the pCMV-II expression vector, transformed into HB101 competent cells and plated onto ampicillin (100 µg/ml). Miniprep analyses led to the identification of the desired clone which was amplified on a larger scale using a Quigen Gigaprep kit following the manufacturer's specifications. The resulting clone was named pCMV.ΔNS35 (Figure 5, SEQ ID NO:3).

pd.ΔNS3NS5: As shown schematically in Figure 10, the yeast expression plasmid pd.ΔNS3NS5 (SEQ ID NO:8) was constructed using restriction fragments obtained from the mammalian expression plasmid pCMV.KM.ΔNS35. pCMV.KM.ΔNS35 is identical to pCMV.ΔNS35 (Figure 5, SEQ ID NO:3) except that it contains a kanamycin resistance gene in the viral backbone. pCMV.KM.ΔNS35 was digested with EcoRI and NheI to obtain 2895bp EcoRI-NheI fragment. EcoRI-NheI

30

fragment was ligated into pRSET HindIII-NheI subcloning vector with oligos (HE) from HindIII to EcoRI. After sequence verification, pRSET HindIII-NheI #6 was digested with HindIII and NheI to obtain a 2908bp HindIII-NheI fragment.

pCMV.KM. Δ NS35 was linearized with XbaI and ligated with synthetic oligos (XS) from XbaI-SalI. The ligation was digested with NheI and SalI to obtain 2481bp NheI-SalI fragment. The fragment was ligated into pET3a NheI-SalI subcloning vector. After sequence verification, pET3a NheI-SalI #2 was digested with NheI and SalI to obtain a 2481bp NheI-SalI fragment. BamHI-HindIII ADH2/GAPDH promoter fragment was then ligated with HindIII-NheI and NheI-SalI fragments into pBS24.1 BamHI-SalI yeast expression vector.

pd. Δ NS3NS5.PJ: pd. Δ NS3NS5.PJ (Figures 13 and 14; SEQ ID NO:10) was generated to create a "perfect junction" at the 5' and 3' end of the HCV coding region. At the 5' end of pd. Δ NS3NS5, there were 6 extra bases between the yeast ADH2/GAPDH promoter and the ATG of the polypeptide. At the 3' end, there were 52 bases of untranslated sequence between the stop codon of the polypeptide and the α -factor terminator in the yeast expression vector. pd. Δ NS3NS5.PJ was created by digesting pd. Δ NS3NS5 #17 with ScaI and SphI to obtain 4963bp ScaI-SphI fragment. pd.NS5b3011 was digested with SphI and SalI to obtain a 321bp SphI-SalI fragment which gave the "perfect junction" at the 3' end of the polypeptide. The ScaI-SphI and SphI-SalI fragments were ligated into pSP72 HindIII-SalI subcloning vector with synthetic oligos from HindIII-ScaI(HS) for the "perfect junction" at the 5' end.

The region of synthetic sequence in pSP72 HindIII-SalI clone# 6 was verified. pSP72 HindIII-SalI clone#6 was digested with HindIII and BlnI or with BlnI and SalI to obtain 2441bp HindIII-BlnI and 2895bp BlnI-SalI fragments, respectively. The BamHI-HindIII ADH2/GAPDH promoter fragment was ligated to HindIII-BlnI and BlnI-SalI fragments into pBS24.1 BamHI-SalI yeast expression vector.

pd. Δ NS3NS5.PJ.core121RT and pd. Δ NS3NS5.PJ.core173RT were generated and encode HCV core aa 1-121 at the C-terminus of the Δ NS3NS5 polypeptide (designated pd. Δ NS3NS5.PJ.core121RT, SEQ ID NO:12) and core aa 1-173 at the C-terminus of the Δ NS3NS5 polypeptide (designated pd. Δ NS3NS5.PJ.core173RT, SEQ ID NO:14). The core sequence had aa 9 mutated from Lys to Arg and aa 11 mutated

from Asn to Thr, designated as core 121RT or 173RT.

pd.ΔNS3NS5.PJ.core121RT and pd.ΔNS3NS5.PJ.core173RT: To generate pd.ΔNS3NS5.PJ.core121RT (Figure 17, SEQ ID NO:12) and pd.ΔNS3NS5.PJ.core173RT (Figure 18, SEQ ID NO:14). As shown in Figure 16, a
5 NotI-SalI HCVcore121RT and HCVcore173RT were amplified by PCR, from an *E. coli* expression plasmid, pSODCF2.HCVcore191RT #2. Either the core 121RT Not-SalI PCR product or the core 173RT Not-SalI PCR product were ligated into a pT7Blue2 PstI-SalI subcloning vector with synthetic oligos (PN) from PstI to NotI. After
10 sequence confirmation, pT7Blue2core121RT clone#9 and pT7Blue2core173RT clone#11 was digested with PstI and SalI to obtain 403bp and 559bp PstI-SalI fragments, respectively, for further cloning.

A 121bp NotI-PstI fragment from pSP72 HindIII-SalI clone #6 was isolated as described above during the cloning of pd.ΔNS3NS5.PJ. NotI-PstI and PstI-SalI fragments were assembled into a vector made by digesting pd.ΔNS3NS5.PJ clone#5
15 (described above) with NotI and SalI.

ΔNS3NS5 and Core 140 and Core 150: An HCV core epitope was found which elicits CTLs in baboons (HCV core aa 121-135). Since pd.ΔNS3NS5.PJ.core121RT ends right before this potentially important epitope and was expressed better than the longer pd.ΔNS3NS5.PJ.core173RT construct (Example 2), two intermediate constructs
20 were made which include this epitope, possibly giving intermediate expression levels. The two new constructs fused HCV core aa 1-140 or HCV core aa1-150 to the C terminus of ΔNS3NS5.PJ.

pd.ΔNS3NS5.PJ.core140RT (Figure 21, SEQ ID NO:16) and pd.ΔNS3NS5.PJ.core150RT (Figure 22, SEQ ID NO:18): As shown in Figure 20, a
25 PstI-SalI HCVcore140RT and a PstI-SalIHCVcore150RT fragment were amplified by PCR from pd.ΔNS3NS5.PJ.core173RT clone #16. Ligate either HCV core PstI-SalI PCR products into pT7Blue2 PstI-SalI subcloning vector. After sequence confirmation, pT7Blue2core140RT clone#22 and pT7Blue2core150RT clone#26 were
30 digested with PstI-SalI to obtain 460bp and 490bp PstI-SalI fragments, respectively, for further cloning.

A 121bp NotI-PstI fragment was isolated from pSP72 HindIII-SalI clone #6 (as described above during the cloning of pd.ΔNS3NS5.PJ. NotI-PstI and PstI-SalI fragments were assembled into a vector made by digesting pd.ΔNS3NS5.PJ clone#5 (described above) with NotI and SalI.

5

Example 2: Protein Expression

Various of the constructs described herein, encoding HCV-1 ΔNS3 to NS5 antigen (aa 1242-3011), were expressed in yeast. *S. cerevisiae* strain AD3 was transformed with pd.ΔNS3NS5 and checked for expression. A stained protein band at the expected molecular weight of 194 kD was not observed (Figure 12). Strain AD3 was also transformed with pd.ΔNS3NS5.PJ clone #5 and checked for expression. A protein band of the expected molecular weight of 194kD was detected (Figure 15).

Strain AD3 was transformed with pd.ΔNS3NS5.PJ.core121RT clone #6 and pd.ΔNS3NS5.PJ.core173RT clone#15 and checked for expression. Protein bands of the expected molecular weight of 206kD and 210kD, respectively, were observed. Expression levels of the pd.ΔNS3NS5.PJ.core173RT construct were much less than that of the pd.ΔNS3NS5.PJ.core121RT construct. (See Figure19). Thus, there is a correlation of protein expression levels and the length of HCV core.

Strain AD3 were transformed with pd.ΔNS3NS5.PJ.core140RT clone# 29 and pd.ΔNS3NS5.PJ.core150RT clone#35 and checked for expression. Bands of the expected molecular weights of 208kD and 209kD were seen by stain at levels close to those of pd.ΔNS3NS5core173RT (Figure 23).

Example 3: Eliciting Immune Responses

A. Immunization

To evaluate the immunogenicity of the mutant NS polypeptides, studies using guinea pigs, rabbits, mice, rhesus macaques and/or baboons are performed. The studies are structured as follows: DNA immunization alone (single or multiple); DNA immunization followed by protein immunization (boost); DNA immunization followed by protein immunization; immunization by PLG particles. Immunization is intramuscular or mucosally.

B. Humoral Immune Response

The humoral immune response is checked in serum specimens from immunized animals with anti-NS antibody ELISAs (enzyme-linked immunosorbent assays) at various times post-immunization. Briefly, serum from immunized animals is screened for antibodies directed against the NS or mutant NS proteins. Wells of ELISA microtiter plates are coated overnight with the selected HCV protein and washed four times; subsequently, blocking is done with PBS-0.2% Tween (Sigma). After removal of the blocking solution, diluted mouse serum is added. Sera are tested at various dilutions. Microtiter plates are washed and incubated with a secondary, peroxidase-coupled anti-mouse IgG antibody (Pierce, Rockford, IL). ELISA plates are washed and 3, 3', 5, 5'-tetramethyl benzidine (TMB; Pierce) is added per well. The optical density of each well is measured. Titers are typically reported as the reciprocal of the dilution of serum that gave a half-maximum optical density (O.D.). Similarly, generation of neutralization of binding (NOB) antibodies can be measured by methods known in the art.

C. Cellular Immune Response

The frequency of specific cytotoxic T-lymphocytes (CTL) is evaluated by a standard chromium release assay of peptide pulsed Balb/c mouse CD4 cells. Briefly, spleen cells (Effector cells, E) are obtained from the BALB/c mice immunized, cultured, restimulated, and assayed for CTL activity against HCV peptide-pulsed target cells. Cytotoxic activity is measured in a standard ^{51}Cr release assay.

Example 4: Immunization with PLG-delivered DNA.

The polylactide-co-glycolide (PLG) polymers are obtained from Boehringer Ingelheim, U.S.A. The PLG polymer is RG505, which has a copolymer ratio of 50/50 and a molecular weight of 65 kDa (manufacturers data). Cationic microparticles with adsorbed DNA are prepared using a modified solvent evaporation process, essentially as described in Singh et al., *Proc. Natl. Acad. Sci. USA* (2000) 97:811-816. Briefly, the microparticles are prepared by emulsifying a 5% w/v polymer solution in methylene chloride with PBS at high speed using an IKA homogenizer. The primary emulsion is

then added to distilled water containing cetyl trimethyl ammonium bromide (CTAB) (0.5% w/v). This results in the formation of a w/o/w emulsion which was stirred at room temperature, allowing the methylene chloride to evaporate. The resulting microparticles are washed in distilled water by centrifugation and freeze dried.

- 5 Following preparation, washing and collection, DNA is adsorbed onto the microparticles by incubating cationic microparticles in a solution of DNA. The microparticles are then separated by centrifugation, the pellet washed with TE buffer and the microparticles are freeze dried, resuspended and administered to animals. Antibody titers are measured by ELISA assays.

10

What is claimed is:

1. An isolated mutant non-structural ("NS") HCV polypeptide comprising a polypeptide having a mutation in the catalytic domain of NS3, wherein said mutation
5 functionally disrupts the catalytic domain.
2. The polypeptide of claim 1, wherein the mutation comprises a deletion.
3. The polypeptide of claim 1, wherein the mutation comprises a
10 substitution.
4. The polypeptide of any of claims 1-3, wherein said NS polypeptide comprises NS3, NS4 and NS5.
- 15 5. The polypeptide of any of claims 1-3, wherein said NS polypeptide consists of NS3, NS4 and NS5.
6. The polypeptide of any of claims 1-3, wherein said NS polypeptide consists of NS3 and NS5.
20
7. The polypeptide of claim 6, wherein NS5 consists of NS5a.
8. The polypeptide of claim 6, wherein NS5 consists of NS5b.
- 25 9. The polypeptide of any of claims 1-3, wherein said NS polypeptide consists of NS3 and NS4.
10. The polypeptide of claim 9, wherein NS4 consists of NS4a.
- 30 11. The polypeptide of claim 9, wherein NS4 consists of NS4b.

12. The polypeptide of claim 4, further comprising a second viral polypeptide that is not NS3, NS4, or NS5 of HCV.

13. The polypeptide of claim 12, wherein the second viral polypeptide
5 comprises an HCV Core polypeptide ("C"), or fragment thereof.

14. The polypeptide of claim 13, wherein the C polypeptide is truncated.

15. The polypeptide of claim 14, wherein the truncation is at amino acid
10 121.

16. The polypeptide of claim 12, wherein the polypeptide further comprises an HCV envelope protein ("E").

17. The polypeptide of claim 16, wherein the E is E1.

18. The polypeptide of claim 16, wherein the E is E2.

19. A composition comprising
20 (a) the polypeptide of any one of claims 1-18; and
(b) a pharmaceutically acceptable excipient.

20. An isolated and purified polynucleotide which encodes the mutant HCV polypeptide according to any one of claims 1-18.

21. A composition comprising
25 (a) the isolated purified polynucleotide of claim 20; and
(b) a pharmaceutically acceptable excipient.

22. The composition of claim 21, wherein the polynucleotide is DNA.

23. The composition of claim 21, wherein the polynucleotide is in a plasmid.
24. An expression vector comprising the polynucleotide of claim 20.
25. An expression vector comprising the polynucleotide of SEQ ID NO:8.
26. A host cell comprising the polynucleotide of claim 20.
27. The host cell of claim 26, wherein the cell is a yeast cell.
28. The host cell of claim 26, wherein the cell is a mammalian cell.
29. The host cell of claim 26, wherein the cell is an insect cell.
30. The host cell of claim 26, wherein the cell is a plant cell.
31. The host cell of claim 26, wherein the polynucleotide comprises the sequence of SEQ ID NO:8.
32. The polypeptide of claim 1, wherein the polypeptide further comprises SEQ ID NO:9.
33. A method of preparing a mutant NS HCV polypeptide, wherein the method comprises the steps of:
- a. transforming a host cell with an expression vector according to claim 24, under conditions wherein the polypeptide is expressed; and
 - b. isolating the polypeptide.

34. The method of claim 33, wherein the host cell is a yeast cell.
35. The method of claim 33, wherein the host cell is a mammalian cell.
- 5 36. The method of claim 33, wherein the host cell is an insect cell.
37. The method of claim 33, wherein the host cell is a plant cell.
38. An antibody that specifically binds to a polypeptide of any of claims 1-
10 18.
39. The antibody of claim 38, wherein the antibody is a monoclonal
antibody.
- 15 40. The antibody of claim 38, wherein the antibody is a purified polyclonal
antibody.
41. A method of eliciting an immune response in a subject, comprising the
step of administering to the subject a polypeptide of any of claims 1-18.
20
42. A method of eliciting an immune response in a subject, comprising the
step of administering to the subject a polynucleotide of claim 20.

Cloning Scheme for Generating pCMV-NS35

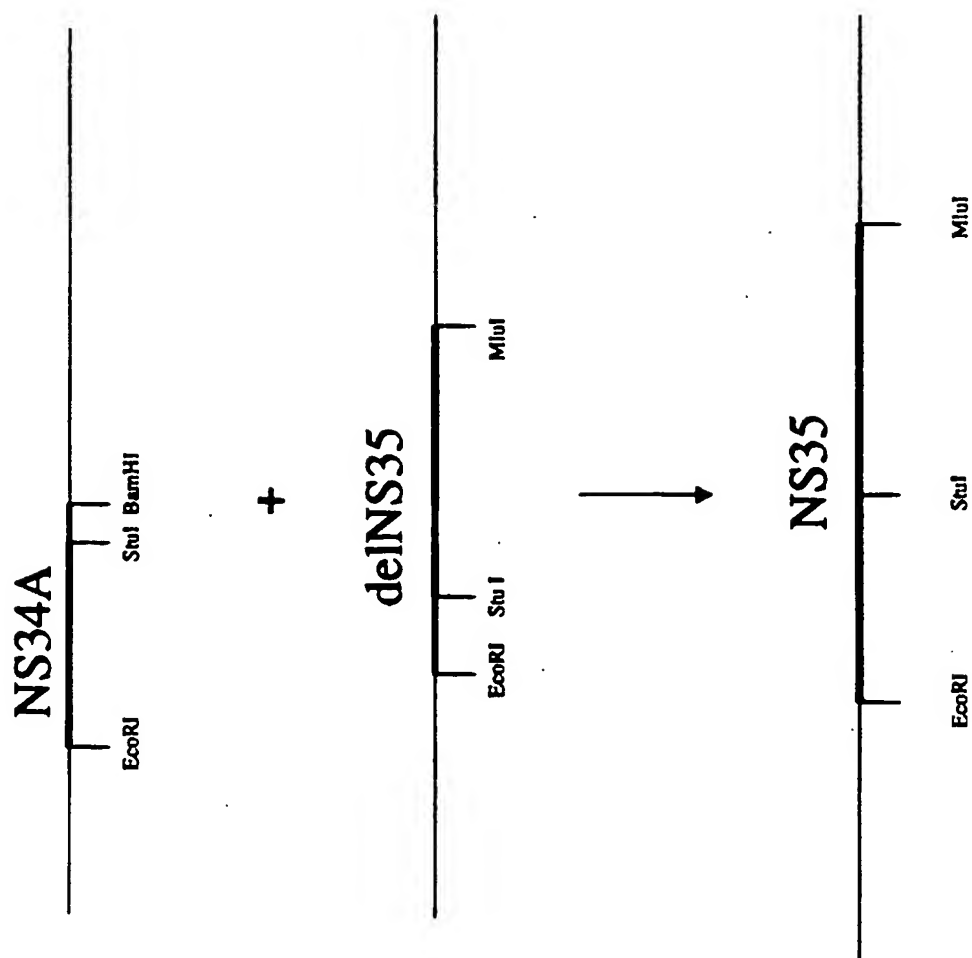
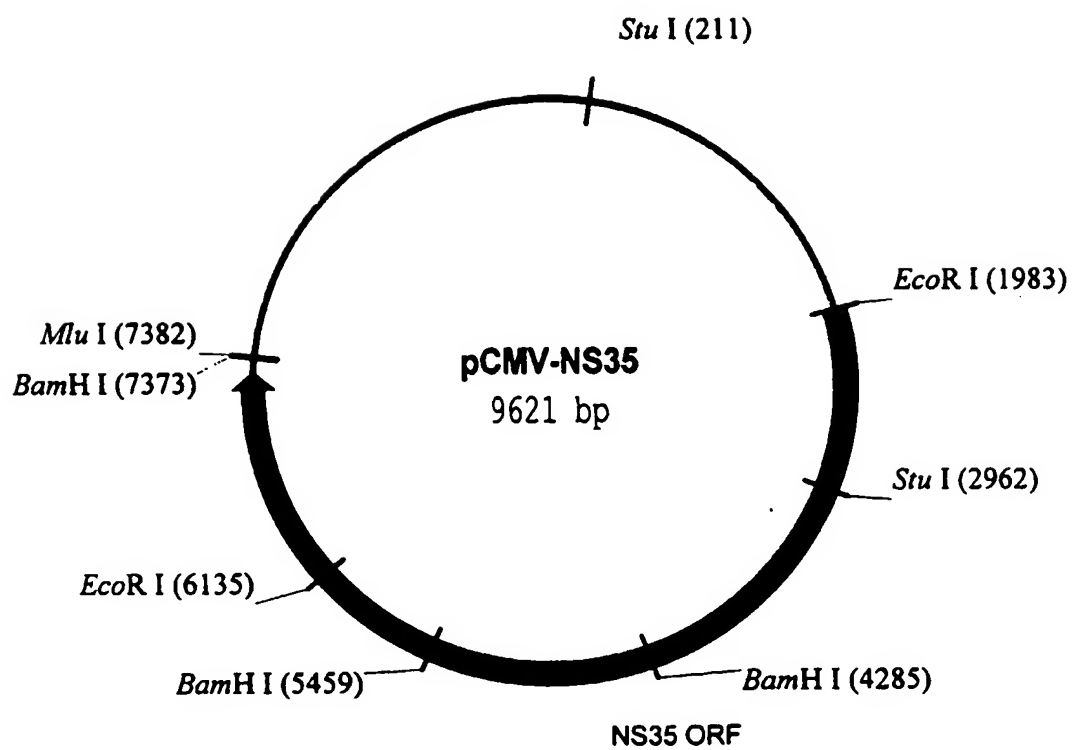


FIGURE 1

FIGURE 2

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FIGURE 3 - Page 1

| | | | | | | | | |
|------|------------|------------|------------|------------|------------|------------|------------|------------|
| 1 | TCGCGCGTTT | CGGTGATGAC | GGTGAAAACC | TCTGACACAT | GCAGCTCCCG | GAGACGGTCA | CAGCTTGTCT | GTAAGCGGAT |
| | AGCGCGCAAA | GCCACTACTG | CCACTTTTGG | AGACTGTGTA | CGTCGAGGGC | CTCTGCCAGT | GTCGAACAGA | CATTGCGCTA |
| 81 | GCCGGGAGCA | GACAAGCCCC | TCAGGGCGCG | TCAGCGGGTG | TTGGCGGGTG | TCGGGGCTGG | CTTAACTATG | CGGCATCAGA |
| | CGGCCCTCGT | CTGTTGCGGC | AGTCCCGCGC | AGTCGCCAC | AACCGCCAC | AGCCCCGACC | GAATTGATAC | GCCGTAGTCT |
| StuI | | | | | | | | |
| 161 | GCAGATTGTA | CTGAGAGTGC | ACCATATGAA | GCTTTTTGCA | AAAGCCTAGG | CCTCCAAAAA | AGCCTCCTCA | CTACTTCTGG |
| | CGTCTAACAT | GACTCTCAGC | TGGTATACTT | CGAAAAACGT | TTTCGGATCC | GGAGGTTTTT | TCGGAGGAGT | GATGAAGACC |
| 241 | AATAGCTCAG | AGGCCGAGGC | GGCCTCGGCC | TCTGCATAAA | TAAAAAAAT | TAGTCAGCCA | TGGGGCGGAG | AATGGGCGGA |
| | TTATCGAGTC | TCCGGCTCCG | CCGGAGCCGG | AGACGTATTT | ATTTTTTTTA | ATCAGTCGGT | ACCCCGCCTC | TTACCCGCTC |
| 321 | ACTGGGCGGG | GAGGGAATTA | TTGGCTATTG | GCCATTCAT | ACGTTGTATC | TATATCATAA | TATGTACATT | TATATTGGCT |
| | TGACCCGCC | CTCCCTTAAT | AACCGATAAC | CGGTAACGTA | TGCAACATAG | ATATAGTATT | ATACATGTAA | ATATAACCGA |
| 401 | CATGTCCAAT | ATGACCGCCA | TGTTGACATT | GATTATTGAC | TAGTTATTAA | TAGTAATCAA | TTACGGGGTC | ATTAGTTCAT |
| | GTACAGGTTA | TACTGGCGGT | ACAACGTAA | CTAATAACTG | ATCAATAATT | ATCATTAGTT | AATGCCCCAG | TAATCAAGTA |
| 481 | AGCCCATATA | TGGAGTTCCG | CGTTACATAA | CTTACGGTAA | ATGGCCCGCC | TGGCTGACCG | CCCAACGACC | CCCGCCCAT |
| | TCGGGTATAT | ACCTCAAGGC | GCAATGTATT | GAATGCCATT | TACCGGGCGG | ACCGACTGGC | GGGTTGCTGG | GGCGGGTAA |
| 561 | GACGTCAATA | ATGACGTATG | TTCCCATAGT | AACGCCAATA | GGGACTTTCC | ATTGACGTCA | ATGGGTGGAG | TATTTACGGT |
| | CTGCAGTTAT | TACTGCATAC | AAGGGTATCA | TTGCGGTTAT | CCCTGAAAGG | TAATGTCAGT | TACCCACCTC | ATAAATGCCA |
| 641 | AAACTGCCCA | CTTGGCAGTA | CATCAAGTGT | ATCATATGCC | AAGTCCGCCC | CCTATTGACG | TCAATGACGG | TAAATGGCCC |
| | TTTGACGGGT | GAACCGTCAT | GTAGTTCACA | TAGTATACGG | TTACGGCGGG | GGATAACTGC | AGTTACTGCC | ATTTACCGGG |
| 721 | GCCTGGCATT | ATGCCAGTA | CATGACCTTA | CGGGACTTTC | CTACTTGGCA | GTACATCTAC | GTATTAGTCA | TCGCTATTAC |
| | CGGACCGTAA | TACGGGTCAT | GTAAGTGAAT | GCCCTGAAAG | GATGAACCGT | CATGTAGATG | CATAATCAGT | AGCGATAATG |
| 801 | CATGGTGATG | CGGTTTTGGC | AGTACACCAA | TGGGCGTGGA | TAGCGGTTTG | ACTCACGGGG | ATTTCCAAGT | CTCCACCCCA |
| | GTACCACTAC | GCCAAAACCG | TCATGTGGTT | ACCCGCACCT | ATCGCCAAAC | TGAGTGCCCC | TAAAGGTTCA | GAGGTGGGGT |
| 881 | TTGACGTCAA | TGGGAGTTTG | TTTTGGCACC | AAAATCAACG | GGACTTTCCA | AAATGTCGTA | ATAACCCCGC | CCCGTTGACG |
| | AACTGCAGTT | ACCCTCAAAC | AAAACCGTGG | TTTTAGTTGC | CCTGAAAGGT | TTTACAGCAT | TATTGGGGCG | GGGCAACTGC |
| 961 | CAAATGGGCG | GTAGGCGTGT | ACGGTGGGAG | GTCTATATAA | GCAGAGCTCG | TTTAGTGAAC | CGTCAGATCG | CCTGGAGACG |
| | GTTTACCCGC | CATCCGCACA | TGCCACCCTC | CAGATATATT | CGTCTCGAGC | AAATCACTTG | GCAGTCTAGC | GGACCTCTGC |
| 1041 | CCATCCACGC | TGTTTTGACC | TCCATAGAAG | ACACCGGGAC | CGATCCAGCC | TCCGCGGGCG | GGAACGGTGC | ATTGGAACGC |
| | GGTAGGTGCG | ACAAAACCTG | AGGTATCTTC | TGTGGCCCTG | GCTAGGTCCG | AGGCGCCGGC | CCTTGCCACG | TAACCTTGCG |
| 1121 | GGATTCCCCG | TGCCAAGAGT | GACGTAAGTA | CGCCTATAG | ACTCTATAGG | CACACCCCTT | TGGCTCTTAT | GCATGCTATA |
| | CCTAAGGGGC | ACGTTTCTCA | CTGCATTCT | GGCGGATATC | TGAGATATCC | GTGTGGGGAA | ACCGAGAATA | CGTACGATAT |
| 1201 | CTGTTTTTGG | CTTGGGGCCT | ATACACCCCC | GCTCCTTATG | CTATAGGTGA | TGGTATAGCT | TAGCCTATAG | GTGTGGGTTA |
| | GACAAAAACC | GAACCCCGGA | TATGTGGGGG | CGAGGAATAC | GATATCCACT | ACCATATCGA | ATCGGATATC | CACACCCAA |
| 1281 | TTGACCATT | TTGACCACTC | CCCTATTGGT | GACGATACTT | TCCATTACTA | ATCCATAACA | TGGCTCTTTG | CCACAACAT |
| | AACTGGTAAT | AACTGGTGAG | GGGATAACCA | CTGCTATGAA | AGGTAATGAT | TAGGTATTGT | ACCGAGAAAC | GGTGTGATA |
| 1361 | CTCTATTGGC | TATATGCCAA | TACTCTGTCC | TTCAGAGACT | GACACGGACT | CTGTATTTT | ACAGGATGGG | GTCCATTTAT |
| | GAGATAACCG | ATATACGGTT | ATGAGACAGG | AAGTCTCTGA | CTGTGCCTGA | GACATAAAAA | TGCTTACCC | CAGGTAATA |

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FIGURE 3 - Page 2

| | | | | | | | | |
|------|------------|-------------|------------|------------|------------|------------|-------------|------------|
| 1441 | TATTTACAAA | TTCACATATA | CAACAACGCC | GTCCCCCGTG | CCCGCAGTTT | TTATTAAACA | TAGCGTGGA | TCTCCGACAT |
| | ATAAATGTTT | AAGTGTATAT | GTTGTTGCGG | CAGGGGGCAC | GGGCGTCAAA | AATAATTTGT | ATCGCACCCCT | AGAGGCTGTA |
| 1521 | CTCGGGTACG | TGTTCCGGAC | ATGGGCTCTT | CTCCGGTAGC | GGCGGAGCTT | CCACATCCGA | GCCCTGGTCC | CATCCGTCCA |
| | GAGCCCATGC | ACAAGGCCCTG | TACCCGAGAA | GAGGCCATCG | CCGCCTCGAA | GGTGTAGGCT | GGGGACCAGG | GTAGGCAGGT |
| 1601 | GCGGCTCATG | GTCGCTCGGC | AGTCCTTGC | TCCTAACAGT | GGAGGCCAGA | CTTAGGCACA | GCACAATGCC | CACCACCACC |
| | CGCCGAGTAC | CAGCGAGCCG | TCGAGGAACG | AGGATTGTCA | CCTCCGGTCT | GAATCCGTGT | CGTGTTACGG | GTGGTGGTGG |
| 1681 | AGTGTGCCGC | ACAAGGCCCT | GGCGGTAGGG | TATGTGTCTG | AAAATGAGCT | CGGAGATTGG | GCTCGCACCT | GGACGCAGAT |
| | TCACACGGCG | TGTTCCGGCA | CCGCCATCCC | ATACACAGAC | TTTTACTCGA | GCCTCTAACC | CGAGCGTGGG | CCTGCGTCTA |
| 1761 | GGAAGACTTA | AGGCAGCGGC | AGAAGAAGAT | GCAGGCAGCT | GAGTTGTGTG | ATTCTGATAA | GAGTCAGAGG | TAACCTCCCT |
| | CCTTCTGAAT | TCCGTCGCCG | TCTTCTTCTA | CGTCCGTCGA | CTCAACAACA | TAAGACTATT | CTCAGTCTCC | ATTGAGGGCA |
| 1841 | TGCGGTGCTG | TTAACGGTGG | AGGGCAGTGT | AGTCTGAGCA | GTAATCGTTG | CTGCCGCGCG | CGCCACCAGA | CATAATAGCT |
| | ACGCCACGAC | AATTGCCACC | TCCCGTCACA | TCAGACTCGT | CATGAGCAAC | GACGGCGCGC | GCGGTGGTCT | GTATTATCGA |
| +2 | | | | | | | M A A | |
| | | | | | | EcoRI | | |
| 1921 | GACAGACTAA | CAGACTGTTT | CTTCCATGG | GTCTTTTCTG | CAGTCACCGT | CGTCGACCTA | AGAATTCACC | ATGGCTGCAT |
| | CTGTCTGATT | GTCTGACAAG | GAAAGGTACC | CAGAAAAGAC | GTCAGTGGCA | GCAGCTGGAT | TCTTAAGTGG | TACCGACGTA |
| +2 | Y A A Q | G Y K | V L V L | N P S | V A A | T L G F | G A Y | M S K |
| 2001 | ATGCAGCTCA | GGGCTATAAG | GTGCTAGTAC | TCAACCCCTC | TGTTGTGTGA | ACACTGGGCT | TGGTGCTTGA | CATGTCCAAG |
| | TACGTCGAGT | CCCGATATTC | CACGATCATG | AGTTGGGGAG | ACAACGACGT | TGTGACCCGA | AACCACGAAT | GTACAGGTTT |
| +2 | A H G I | D P N | I R T | G V R T | I T T | G S P | I T Y S | T Y G |
| 2081 | GCTCATGGGA | TCGATCCTAA | CATCAGGACC | GGGGTGAGAA | CAATTACCAC | TGGCAGCCCC | ATCAGCTACT | CCACCTACGG |
| | CGAGTACCCT | AGCTAGGATT | GTAGTCTCTG | CCCCACTCTT | GTTAATGGTG | ACCGTCGGGG | TAGTGATGA | GGTGGATGCC |
| +2 | K F L | A D G G | C S G | G A Y | D I I I | C D E | C H S | T D A |
| 2161 | CAAGTTCCTT | GCCGACGGCG | GGTGCTCGGG | GGGCGCTTAT | GACATAATAA | TTTGTGACGA | GTGCCACTCC | ACGGATGCCA |
| | GTTCAAGGAA | CGGCTGCCGC | CCACGAGCCC | CCCGCGAATA | CTGTATTATT | AAACTGTCT | CACGGTGAGG | TGCTACGGT |
| +2 | T S I L | G I G | T V L D | Q A E | T A G | A R L V | V L A | T A T |
| 2241 | CATCACTCTT | GGGCATTGGC | ACTGTCTCTG | ACCAAGCAGA | GACTGCGGGG | GCGAGACTGG | TTGTGCTCGC | CACCGCCACC |
| | GTAGGTAGAA | CCCGTAACCG | TGACAGGAAC | TGTTCTGTCT | CTGACGCCCC | CGCTCTGACC | AACACGAGCG | GTGGCGGTGG |
| +2 | P P G S | V T V | P H P | N I E E | V A L | S T T | G E I P | F Y G |
| 2321 | CCTCCGGGCT | CCGTCACGTG | GCCCCATCCC | AACATCGAGG | AGGTTGCTCT | GTCCACCACC | GGAGAGATCC | CTTTTACGG |
| | GGAGGCCCGA | GGCAGTGACA | CGGGGTAGGG | TTGTAGCTCC | TCCAACGAGA | CAGGTGGTGG | CCTCTCTAGG | GAAAAATGCC |
| +2 | K A I | P L E V | I K G | G R H | L I F C | H S K | K K C | D E L |
| 2401 | CAAGGCTATC | CCCCTCGAAG | TAATCAAGGG | GGGGAGACAT | CTCATCTTCT | GTCATTCAAA | GAAGAAGTGC | GACGAACCTG |
| | GTTCCGATAG | GGGGAGCTTC | ATTAGTTCCC | CCCCTCTGTA | GAGTAGAAGA | CAGTAAGTTT | CTTCTTCACG | CTGCTTGAGC |
| +2 | A A K L | V A L | G I N A | V A Y | Y R G | L D V S | V I P | T S G |
| 2481 | CCGCAAGGCT | GGTCGCATTG | GGCATCAATG | CCGTGGCCTA | CTACCGCGGT | CTTGACGTGT | CCGTCATCCC | GACCAGCGGC |
| | GGCGTTTCGA | CCAGCGTAAC | CCGTAGTTAC | GGCACCGGAT | GATGGCGCCA | GAACGTGACA | GGCAGTAGGG | CTGGTCGCCG |
| +2 | D V V V | V A T | D A L | M T G Y | T G D | F D S | V I D C | N T C |
| 2561 | GATGTTGTG | TCGTGGCAAC | CGATGCCCTC | ATGACCGGCT | ATACCGGCGA | CTTCGACTCG | GTGATAGACT | GCAATACGTG |
| | CTACAACAGC | AGCACCGTTG | GCTACGGGAG | TACTGGCCGA | TATGGCCGCT | GAAGCTGAGC | CACTATCTGA | CGTTATGCAC |

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FIGURE 3 - Page 3

+2 V T Q T V D F S L D P T F T I E T I T L P Q D A V S
 2641 . TGTCACCCAG ACAGTCGATT TCAGCCTTGA CCCTACCTTC ACCATTGAGA CAATCACGCT CCCCCAAGAT GCTGTCTCCC
 ACAGTGGGTC TGTCAGCTAA AGTCGGAAC GGGATGGAAG TGGAACCTCT GTTAGTGCGA GGGGGTCTA CGACAGAGGG

+2 R T Q R R G R T G R G K P G I Y R F V A P G E R P S G
 2721 GCACTCAACG TCGGGGCAGG ACTGGCAGGG GGAAGCCAGG CATCTACAGA TTTGTGGCAC CGGGGGAGCG CCCCTCCGGC
 CGTGAGTTGC AGCCCCGTCC TGACCGTCCC CTTTCGGTCC GTAGATGTCT AAACACCGTG GCCCCTCGC GGGGAGGCCG

+2 M F D S S V L C E C Y D A G C A W Y E L T P A E T T V
 2801 ATGTTCTGACT CGTCCGTCCT CTGTGAGTGC TATGACGCAG GCTGTGCTTG STATGAGCTC ACGCCCGCCG AGACTACAGT
 TACAAGCTGA GCAGGCAGGA GACACTCAGC ATACTCGCTC CGACACGAAC CATACTCGAG TCGGGGCGGC TCTGATGTCA

+2 R L R A Y M N T P G L P V C Q D H L E F W E G V F T
 StuI
 2881 TAGGCTACGA GCGTACATGA ACACCCCGGG GCTTCCCGTG TGCCAGGACC ATCTTGAATT TTGGGAGGGC GTCTTTACAG
 ATCCGATGCT CGCATGTACT TGTGGGGCCC CGAAGGGCAC ACGGTCCTGG TAGAACTTAA AACCTCCCG CAGAAATGTC

+2 G L T H I D A H F L S Q T K Q S G E N L P Y L V A Y Q
 StuI
 2961 GCCTCACTCA TATAGATGCC CACTTCTAT CCCAGACAAA GCAGAGTGGG GAGAACCCTC CTTACCTGGT AGCGTACCAA
 CGGAGTGAGT ATATCTACGG GTGAAAGATA GGGTCTGTTT CGTCTCACCC CTCTTGAAG GAATGGACCA TCGCATGGT

+2 A T V C A R A Q A P P P S W D Q M W K C L I R L K P T
 3041 GCCACCGTGT GCGCTAGGGC TCAAGCCCCT CCCCATCGT GGGACCAGAT GTGGAAGTGT TTGATTCCGC TCAAGCCAC
 CGGTGGCACA CGCGATCCCG AGTTCGGGGA GGGGGTAGCA CCCTGGTCTA CACCTTCACA AACTAAGCGG AGTTCGGGTG

+2 L H G P T P L L Y R L G A V Q N E I T L T H P V T K
 3121 CCTCCATGGG CCAACACCCC TGCTATACAG ACTGGGCGCT GTTCAGAATG AAATCACCTT GACGCACCCA GTCACCAAT
 GGAGGTACCC GGTGTGGGG ACGATATGTC TGACCCGCGA CAAGTCTTAC TTTAGTGGA CTGCGTGGT CAGTGGTTA

+2 Y I M T C M S A D L E V V T S T W V L V G G V L A A L
 3201 ACATCATGAC ATGCTATGCG GCCGACCTGG AGGTCGTAC GAGCACCTGG GTGCTCGTTG GCGGCGTCTT GCGTGGTTG
 TGTAGTACTG TACGTACAGC CGGCTGGACC TCCAGCAGTG CTCGTGGACC CACGAGCAAC CGCCGAGGA CCGACGAAC

+2 A A Y C L S T G C V V I V G R V V L S G K P A I I P D
 3281 GCCCGGTATT GCCTGTCAAC AGGCTGCGTG GTCATAGTGG GCAGGGTCTT CTTGTCCGGG AAGCCGGCAA TCATACCTGA
 CGGCGCATAA CGGACAGTTG TCCGACGCAC CAGTATCACC CGTCCAGCA GAACAGGCC TTCCGGCGTT AGTAGGACT

+2 R E V L Y R E F D E M E E C S Q H L P Y I E Q G M M
 3361 CAGGGAAGTC CTCTACCGAG AGTTCGATGA GATGGAAGAG TGCTCTCAGC ACTTACCGTA CATCGAGCAA GGGATGATGC
 GTCCCTTCAG GAGATGGCTC TCAAGCTACT CTACCTTCTC ACGAGAGTGC TGAATGGCAT GTAGCTCGTT CCCTACTACG

+2 L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V
 3441 TCGCCGAGCA GTTCAAGCAG AAGGCCCTCG GCCTCTGCA GACCCGCTCC CGTCAGGCAG AGGTTATCGC CCCTGCTGTC
 AGCGGCTCGT CAAGTTCTGTC TTCCGGGAGC CGGAGGACGT CTGGCGCAGG GCAGTCCGTC TCCAATAGCG GGGACGACAG

+2 Q T N W Q K L E T F W A K H M W N F I S G I Q Y L A G
 3521 CAGACCACT GGCRAAACT CGAGACCTTC TGGGCGAAGC ATATGTGGAA CTTATCAGT GGGATACAAT ACTTGGCGGG
 GTCTGGTTGA CCGTTTTTGA GCTCTGGAAG ACCCGCTTC TATACACCTT GAAGTAGTCA CCCTATGTTA TGAACCGCC

+2 L S T L P G N P A I A S L M A F T A A V T S P L T T
 3601 CTTGTCAACG CTGCCTGGTA ACCCCGCCAT TGCTTCATTG ATGGCTTTTA CAGCTGCTGT CACCAGCCCA CTAACCACTA
 GAACAGTTGC GACGGACCAT TGGGGCGGTA ACGAAGTAAC TACCGAAAT GTCGACGACA GTGGTGGGT GATTGGTGAT

+2 S Q T L L F N I L G G W V A A Q L A A P G A A T A F V
 3681 GCCAAACCTT CCTCTCAAC ATATTGGGGG GGTGGGTGGC TGCCAGCTC GCCGCCCGG GTGCCGCTAC TGCCCTTGTG
 CGGTTTGGGA GGAGAAGTTG TATAACCCC CCACCCACCG ACGGTCGAG CGCGGGGGC CACGGCGATG ACGGAACAC

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FIGURE 3 - Page 4

+2 G A G L A G A A I G S V G L G K V L I D I L A G Y G A
 3761 GGGCGTGGCT TAGCTGGCGC CGCCATCGGC AGTGTGGAC TGGGGAAGGT CCTCATAGAC ATCCTTGAG GGTATGGCGC
 CCGCGACCGA ATCGACCGCG GCGGTAGCCG TCACAACCTG ACCCCTTCCA GGAGTATCTG TAGGAACGTC CCATACCGCG

+2 G V A G A L V A F K I M S G E V P S T E D L V N L L
 3841 GGGCGTGGCG GGAGCTCTTG TGGCATTCAA GATCATGAGC GGTGAGGTCC CCTCCACGGA GGACCTGGTC AATCTACTGC
 CCCGACCGC CCTCGAGAAC ACCGTAAGTT CTAGTACTCG CCACTCCAGG GGAGGTGCCT CTGGGACCAG TTAGATGACG

+2 P A I L S P G A L V V G V V C A A I L R R H V G P G E
 3921 CCGCATCTCT CTCGCCCGGA GCCCTCGTAG TCGGCGTGGT CTGTGCAGCA ATACTGCGCC GGCACGTTGG CCCGGGCGAG
 GGGGTAGGA GAGCGGGCCT CGGAGCATC AGCCGCACCA GACACGTCGT TATGACGCGG CCGTGCAACC GGGCCCCGCT

+2 G A V Q W M N R L I A F A S R G N H V S P T H Y V P E
 4001 GGGGCGTGC AGTGGATGAA CCGGCTGATA GCCTTCGCT CCCGGGGGAA CCATGTTTCC CCCACGCACT ACGTGCCGGA
 CCGGCTACG TCACCTACTT GCGCGACTAT CGGAAGCGGA GGGCCCCCTT GGTACAAAGG GGGTGCCTGA TGCACGGCCT

+2 S D A A A R V T A I L S S L T V T Q L L R R L H Q W
 4081 GAGCGATGCA GGTGCCCCGCG TCACTGCCAT ACTCAGCAGC CTCACTGTAA CCCAGCTCCT GAGGCGAGTG CACCAGTGGA
 CTCGCTACGT CGACGGGCGC AGTGACGGTA TGAGTCGTG GAGTGACATT GGGTCGAGGA CTCGCTGAC GTGGTCACCT

+2 I S S E C T T P C S G S W L R D I W D W I C E V L S D
 4161 TAAGCTCGGA GTGTACCACT CCATGCTCCG GTTCTGCTT AAGGGACATC TGGGACTGGA TATGCGAGGT GTTGAGCGAC
 ATTCGAGCCT CACATGGTGA GGTACGAGG CAAGGACCGA TTCCCTGTAG ACCCTGACCT ATACGCTCCA CAACCTCGTG

+2 F K T W L K A K L M P Q L P G I P F V S C Q R G Y K G
 BamHI
 4241 TTTAAGACCT GGCTAAAAGC TAAGCTCATG CCACAGCTGC CTGGGATCCC CTTTGTGTCC TGCCAGCGCG GGTATAAGGG
 AAATTCTGGA CCGATTTTCG ATTCGAGTAC GGTGTGACG GACCCTAGGG GAAACACAGG ACGGTGCGCG CCATATTCCC

+2 V W R G D G I M H T R C H C G A E I T G H V K N G T
 4321 GGTCTGGCGA GGGGACGGCA TCATGCACAC TCGTCCGAC TGTGGAGCTG AGATCACTGG ACATGICAAA AACGGGACGA
 CCGACCGCT CCCCTGCCGT AGTACGTGTG AGCGACGGTG ACACCTCGAC TCTAGTGACC TGTACAGTTT TTGCCCTGCT

+2 M R I V G P R T C R N M W S G T F P I N A Y T T G P C
 4401 TGAGGATCGT CGGTCTTAGG ACCTGCAGGA ACATGTGGAG TGGGACCTTC CCCATTAATG CCTACACCAAC GGGCCCCCTGT
 ACTCTAGCA GCCAGGATCC TGGACGTCCT TGTACACCTC ACCCTGGAAG GGGTAATTAC GGATGTGGTG CCCGGGGACA

+2 T P L P A P N Y T F A L W R V S A E E Y V E I R Q V G
 4481 ACCCCCTTC CTGCGCCGAA CTACACGTTT GCGCTATGGA GGTGTCTGCG AGAGGAATAC GTGGAGATAA GGCAGGTGGG
 TGGGGGGAAG GACGCGGCTT GATGTGCAAG CGCGATACCT CCCACAGACG TCTCCTTATG CACCTCTATT CCGTCCACCC

+2 D F H Y V T G M T T D N L K C P C Q V P S P E F F T
 4561 GGACTTCCAC TACGTGACGG GTATGACTAC TGACAATCTT AAATGCCCGT GCCAGGTCCC ATCGCCCGAA TTTTTCACAG
 CCTGAAGGTG ATGCACTGCC CATACTGATG ACTGTTAGAA TTTACGGGCA CGGTCCAGGG TAGCGGGCTT AAAAAGTGTC

+2 E L D G V R L H R F A P P C K P L L R E E V S F R V G
 4641 AATTGGACGG GGTGCGCCTA CATAGGTTTG CGCCCCCTG CAAGCCCTTG CTGCGGGAGG AGGTATCATT CAGAGTAGGA
 TTAACCTGCC CCACGCGGAT GTATCCAAAC GCGGGGGGAC GTTCGGGAAC GACGCCCTCC TCCATAGTAA GTCTCATCTT

+2 L H E Y P V G S Q L P C E P E P D V A V L T S M L T D
 4721 CTCCACGAAT ACCCGGTAGG GTCGCAATTA CCTTGCAGC CCGAACCGGA CGTGGCCGTG TTGACGTCCA TGCTCACTGA
 GAGGTGCTTA TGGGCGATCC CAGCGTTAAT GGAACGCTCG GGCTTGGCCT GCACCGGCAC AACTGCAGGT ACGAGTGACT

+2 P S H I T A E A A G R R L A R G S P P S V A S S S A
 4801 TCCCTCCCAT ATAACAGCAG AGGCGGGCGG GCGAAGGTTG GCGAGGGGAT CACCCCTCTG TGTGGCCAGC TCCTCGGCTA
 AGGAGGGTA TATTGTGTCG TCCGCGGGC CGCTTCCAAC CGCTCCCCTA GTGGGGGGAG ACACCGGTG AGGAGCGGAT

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FIGURE 3 - Page 5

+2 S Q L S A P S L K A T C T A N H D S P D A E L I E A N
 4881 GCCAGCTATC CGCTCCATCT CTCAGGCAA CTTGCACGGC TAACCATGAC TCCCCTGATG CTGAGCTCAT AGAGGCCAAC
 CGGTCGATAG GCGAGGTAGA GAGTCCGTT GAACGTGGCG ATTGGTACTG AGGGGACTAC GACTCGAGTA TCTCCGGTTG

+2 L L W R Q E M G G N I T R V E S E N K V V I L D S F D
 4961 CTCCTATGGA GGCAGGAGAT GGGCGGCAAC ATCACCAGGG TTGAGTCAGA AAACAAAGTG GTGATTCTGG ACTCCTTCGA
 GAGGATACCT CCGTCCTCTA CCCGCCGTTG TAGTGGTCCC AACTCAGTCT TTTGTTTCAC CACTAAGACC TGAGGAAGCT

+2 P L V A E E D E R E I S V P A E I L R K S R R F A Q
 5041 TCCGCTTGTG GCGGAGGAGG ACGAGCGGGA GATCTCCGTA CCCGAGAGAA TCCTGCGGAA GTCTCGGAGA TTCGCCCAGG
 AGGCGAACAC CGCTCCTCC TGCTCGCCCT CTAGAGGCAT GGGCGTCTTT AGGACGCCCT CAGAGCCTCT AAGCGGGTCC

+2 A L P V W A R P D Y N P P L V E T W K K P C Y E P P V
 5121 CCCTGCCCCG TTGGGCGCGG CCGGACTATA ACCCCCGCT AGTGGAGACG TGGAAAAGC CCGACTACGA ACCACCTGTG
 GGGACGGGCA AACCCGCGCC GGCCTGATAT TGGGGGCGCA TCACCTCTGC ACCTTTTTTCG CGGTATGCT TGGTGGACAC

+2 V H G C P L P P P K S P P V P P P R K K R T V V L T E
 5201 GTCCATGGCT GCCCGCTTCC ACCTCCAAAG TCCCCTCTG TGCTCCGCC TCAGAAAGAG CCGACGGTGA GTCTCACTGA
 CAGGTACCGA CGGGCGAAGG TGGAGGTTTC AGGGGAGGAC ACGGAGGCGG AGCCTTCTTC GCCTGCCACC AGGAGTACT

+2 S T L S T A L A E L A T R S F G S S S T S G I T G D
 5281 ATCAACCTTA TCTACTGCCT TGGCCGAGCT CGCCACCAGA AGCTTTGGCA GCTCCTCAAC TTCCGGCATT ACGGGCGACA
 TAGTTGGGAT AGATGACGGA ACCGGCTCGA GCGGTGGTCT TCGAAACCGT CGAGGAGTTG AAGGCCGTAA TGCCCGTGT

+2 N T T T S S E P A P S G C P P D S D A E S Y S S M P P
 5361 ATACGACAAC ATCCTCTGAG CCCGCCCTT CTGGCTGCCC CCCCGACTCC GACGCTGAGT CCTATTCTCT CATGCCCCCC
 TATGCTGTG TAGGAGACTC GGGCGGGGAA GACCGACGGG GGGGCTGAGG CTGCGACTCA GGATAAGGAG GTACGGGGGG

+2 L E G E P G D P D L S D G S W S T V S S E A N A E D V
 BamHI
 ~~~~~  
 5441 CTGGAGGGGG AGCCTGGGGA TCCGGATCTT AGCGACGGGT CATGGTCAAC GGTCAAGTAGT GAGGCCAACG CGGAGGATGT  
 GACCTCCCCC TCGGACCCCT AGGCCTAGAA TCCTGCCCCA GTACCAGTTG CCAGTCATCA CTCGGTTGCG GCCTCCTACA

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+2 V C C S M S Y S W T G A L V T P C A A E E Q K L P I  
 5521 CGTGTGCTGC TCAATGTCTT ACTCTTGGAC AGGCGCACTC GTCACCCCGT GCGCCGCGGA AGAACAGAAA CTGCCCATCA  
 GCACACGACG AGTTACAGAA TGAGAACCTG TCCGCGTGAG CAGTGGGGCA CGCGGCGCCT TCTGTCTTT GACGGGTAGT

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+2 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K  
 5601 ATGCACTAAG CAACTCGTTG CTACGTCACC ACAATTGGT GTATTCCACC ACCTCACGCA GTGCTTGCCA AAGGCAGAAG  
 TACGTGATTC GTTGAGCAAC GATGCAGTGG TGTTAAACCA CATAAGGTGG TGGAGTGCGT CACGAACCGT TTCCGTCCTC

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+2 K V T F D R L Q V L D S H Y Q D V L K E V K A A A S K  
 5681 AAAGTCACAT TTGACAGACT GCAAGTTCTG GACAGCCATT ACCAGGACGT ACTCAAGGAG GTTAAAGCAG CGGCGTCAAA  
 TTTCAGTGTA AACTGTCTGA CGTTCAAGAC CTGTGCGTAA TGGTCTGCA TGAGTTCTC CAATTTCGTC GCCGCGTCT

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+2 V K A N L L S V E E A C S L T P P H S A K S K F G Y  
 5761 AGTGAAGGCT AACTTGCTAT CCGTAGAGGA AGCTTGCAGC CTGACGCCCC CACACTCAGC CAAATCCAAG TTTGGTTATG  
 TCACTTCCGA TTGAACGATA GGCATCTCCT TCGAACGTCG GACTGCGGGG GTGTGAGTCG GTTTAGGTTC AAACCAATAC

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+2 G A K D V R C H A R K A V T H I N S V W K D L L E D N  
 5841 GGGCAAAAGA CGTCCGTTGC CATGCCAGAA AGGCCGTAAC CCACATCAAC TCCGTGTGGA AAGACCTTCT GGAAGACAAT  
 CCCCCTTTCT GCAGGCAACG GTACGGTCTT TCCGGCATTG GGTGTAGTTG AGGCACACCT TTCTGGAAGA CCTTCTGTTA

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+2 V T P I D T T I M A K N E V F C V Q P E K G G R K P A  
 5921 GTAACACCAA TAGACACTAC CATCATGGCT AAGAAGCAGG TTTTCTGCGT TCAGCCTGAG AAGGGGGGTC GTAAGCCAGC  
 CATTGTGGTT ATCTGTGATG GTAGTACCGA TTCTGTCTCC AAAAGACGCA AGTCGGAATC TTCCCCCAG CATTGCTGTC

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## FIGURE 3 - Page 6

+2 R L I V F P D L G V R V C E K M A L Y D V V T K L P  
 6001 TCGTCTCATC GTGTTCCCGG ATCTGGGCGT GCGCGTGTGC GAAAGATGG CTTTGTACGA CGTGGTTACA AAGTCCCCT  
 AGCAGAGTAG CACAAGGGGC TAGACCCGCA CGCGCACAG CTTTCTACC GAAACATGCT GCACCAATGT TTCAGAGGGA

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+2 L A V M G S S Y G F Q Y S P G Q R V E F L V Q A W K S  
 EcoRI  
 -----  
 6081 TGGCCGTGAT GGAAGCTCC TACGGATTCC AATACTACC AGGACAGCGG GTTGAATTCC TCGTGCAAGC GTGGAAGTCC  
 ACCGGCACTA CCCTTCGAGG ATGCCTAAGG TTATGAGTGG TCCTGTCGCC CAACTTAAGG AGCACGTTCC CACCTTCAGG

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+2 K K T P M G F S Y D T R C F D S T V T E S D I R T E E  
 6161 AAGAAAACCC CAATGGGGTT CTCGTATGAT ACCCGCTGCT TTGACTCCAC AGTCACTGAG AGCGACATCC GTACGGAGGA  
 TTCCTTTGGG GTTACCCCAA GAGCATACTA TGGCGACGA AACTGAGGTG TCAGTGACTC TCGCTGTAGG CATGCCCTCT

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+2 A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G  
 6241 GGCAATCTAC CAATGTTGTG ACCTCGACCC CCAAGCCCGC GTGGCCATCA AGTCCCTCAC CGAGAGGCTT TATGTTGGG  
 CCGTTAGATG GTTACAACAC TGGAGCTGGG GGTTCGGGCG CACCGTAGT TCAGGGAGTG GCTCTCCGAA ATACAACCC

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+2 G P L T N S R G E N C G Y R R C R A S G V L T T S C G  
 6321 GCCCTCTTAC CAATTCAAGG GGGGAGAACT GCGGCTATCG CAGGTGCCG GCGAGCGCG TACTGACAAC TAGCTGTGGT  
 CGGGAGAATG GTTAAGTTCC CCCCTCTGA CGCGATAGC GTCCACGGCG CGCTCGCGC ATGACTGTTG ATCGACACCA

---

+2 N T L T C Y I K A R A A C R A A G L Q D C T M L V C G  
 6401 AACACCCTCA CTTGCTACAT CAAGGCCCGG GCAGCCTGTC GAGCCGCGG GCTCCAGGAC TGCACCATGC TCGTGTGGG  
 TTGTGGGAGT GAACGATGTA GTTCCGGGCC CGTCGGACAG CTCGGCGTCC CGAGGTCTCTG ACGTGGTACG AGCACACACC

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+2 D D L V V I C E S A G V Q E D A A S L R A F T E A M  
 6481 CGACGACTTA GTCGTATCT GTGAAAGCGG GGGGCTCCAG GAGGACGCGG CGAGCCTGAG AGCCTTCACG GAGGCTATGA  
 GCTGTGAAT CAGCAATAGA CACTTTCGCG CCCCAGGTC CTCCTGCGCC GCTCGGACTC TCGGAAGTGC CTCGATACT

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+2 T R Y S A P P G D P P Q P E Y D L E L I T S C S S N V  
 6561 CCAGGTACTC CGCCCCCT GGGGACCCG CACAACCAGA ATACGACTTG GAGCTCATAA CATCATGCTC CTCACACGTG  
 GTTCCATGAG GCGGGGGGA CCCCTGGGG GTGTTGGTCT TATGCTGAAC CTCGAGTATT GTAGTACGAG GAGGTTGCAC

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+2 S V A H D G A G K R V Y Y L T R D P T T P L A R A A W  
 6641 TCAGTCGCCC ACGACGGCGG TGGAAGAGG GTCTACTACC TCACCCGTGA CCCTACAACC CCCCTCGCGA GAGTGCCTG  
 AGTCAGCGG TGCTGCCGCG ACCTTCTCC CAGATGATGG AGTGGGCACT GGGATGTTGG GGGGAGCGCT CTCGACGCAC

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+2 E T A R H T P V N S W L G N I I M F A P T L W A R M  
 6721 GGAGACAGCA AGACACACTC CAGTCAATTC CTGGCTAGGC AACATAATCA TGTGTCCTC CACACTGTGG GCGAGGATGA  
 CCTCTGTCGT TCTGTGTGAG GTCAGTTAAG GACCGATCCG TTGTATTAGT ACAAACGGGG GTGTGACACC CGCTCTACT

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+2 I L M T H F F S V L I A R D Q L E Q A L D C E I Y G A  
 6801 TACTGATGAC CCATTTCTTT AGCGTCCTTA TAGCCAGGGA CCAGCTTGAA CAGGCCCTCG ATTGCGAGAT CTACGGGGG  
 ATGACTACTG GGTAAAGAAA TCGCAGGAAT ATCGGTCCCT GGTGCAACTT GTCCGGGAGC TAACGCTCTA GATGCCCCG

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+2 C Y S I E P L D L P P I I Q R L H G L S A F S L H S Y  
 6881 TGCTACTCCA TAGAACCCTT GGATCTACCT CCAATCATTC AAAGACTCCA TGGCCTCAGC GCATTTTCAC TCCACAGTTA  
 ACGATGAGGT ATCTTGGTGA CCTAGATGGA GGTTAGTAAG TTTCTGAGGT ACCGGAGTCG CGTAAAAGTG AGGTGTCAAT

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+2 S P G E I N R V A A C L R K L G V P P L R A W R H R  
 6961 CTCTCCAGGT GAAATCAATA GGGTGGCCG ATGCCTCAGA AAAGTTGGG TACCGCCCTT GCGAGCTTGG AGACACCGG  
 GAGAGGTCCA CTTAGTTAT CCCACCGCG TACGAGTCT TTTGAACCC ATGGCGGGA CGCTCGAACC TCTGTGGCC

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+2 A R S V R A R L L A R G G R A A I C G K Y L F N W A V  
 7041 CCCGAGCGT CCGCGTAGG CTTCTGGCCA GAGGAGGCG GGCTGCCATA TGTGGCAAGT ACCTCTTCAA CTGGGCGTA  
 GGGCTCGCA GCGCGATCC GAAGACCGT CTCTCCGTC CCGACGGTAT ACACGTTCA TGGAGAAGTT GACCCGTCAT

**FIGURE 3 - Page 7**

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## FIGURE 3 - Page 8

8481 ATCTTCACCT AGATCCTTTT AAATTAAAAA TGAAGTTTTA AATCAATCTA AAGTATATAT GAGTAAACTT GGTCTGACAG  
TAGAAGTGGA TCTAGGAAAA TTTAATTTTT ACTTCAAAAT TTAGTTAGAT TTCATATATA CTCATTTGAA CCAGACTGTC

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8561 TTACCAATGC TTAATCAGTG AGGCACCTAT CTCAGCGATC TGTCTATTTC GTTCATCCAT AGTTGCCTGA CTCCTCGTCG  
AATGGTTACG AATTAGTCAC TCCGTGGATA GAGTCGCTAG ACAGATAAAG CAAGTAGGTA TCAACGGACT GAGGGGCAGC

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8641 TGTAGATAAC TACGATACGG GAGGGCTTAC CATCTGGCCC CAGTGCTGCA ATGATACCGC GAGACCCACG CTCACCGGCT  
ACATCTATTG ATGCTATGCC CTCCCGAATG GTAGACCGGG GTCACGACGT TACTATGGCG CTCTGGGTGC GAGTGGCCGA

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8721 CCAGATTTAT CAGCAATAAA CCAGCCAGCC GGAAGGGCCG AGCGCAGAAG TGGTCCTGCA ACTTTATCCG CCTCCATCCA  
GGTCTAAATA GTCGTTATTT GGTGCGTCGG CCTTCCCGGC TCGCGTCTTC ACCAGGACGT TGAAATAGGC GGAGGTAGGT

---

8801 GTCTATTAAT TGTGGCCGGG AAGCTAGAGT AAGTAGITCG CCAGTTAATA GTTTCGCGAA CGTTGTGGCC ATTGCTACAG  
CAGATAATTA ACAACGGCCC TTCGATCTCA TTCATCRAAG GGTCAATTAT CAAACGCGTT GCAACAACGG TAACGATGTC

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8881 GCATCGTGGT GTCACGCTCG TCGTTTGGTA TGCTTCATT CAGTCCGGT TCCCAACGAT CAAGGCGAGT TACATGATCC  
CGTAGCACCA CAGTGCAGC AGCAAACCAT ACCGAAGTAA GTCGAGGCCA AGGGTTGCTA GTTCCGCTCA ATGTACTAGG

---

8961 CCCATGTTGT GCAAAAAAGC GGTAGCTCC TTCGGTCCTC CGATCGTTGT CAGAAGTAAG TTGGCCGCGT TGTATCACT  
GGGTACAACA CGTTTTTTCG CCAATCGAGG AAGCCAGGAG GCTAGCAACA GTCTTCATT AACC GGCGTC ACAATAGTGA

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9041 CATGGTTATG GCAGCACTGC ATAATCTCT TACTGTCATG CCATCCGTAA GATGCTTTTC TGTGACTGGT GAGTACTCAA  
GTACCAATAC CGTCGTGACG TATTAAGAGA ATGACAGTAC GGTAGGCATT CTACGAAAAG ACACTGACCA CTCATGAGTT

---

9121 CCAAGTCATT CTGAGAATAG TGTATGCGGC GACCGAGTTG CTCTTGCCCG GCGTCAATAC GGGATAATAC CGCGCCACAT  
GGTTCAGTAA GACTCTTATC ACATACGCCG CTGGCTCAAC GAGAACGGGC CGCAGTTATG CCCTATTATG GCGCGGTGTA

---

9201 AGCAGAACTT TAAAAGTGCT CATCATTGGA AAACGTCTT CGGGGCGAAA ACTCTCAAGG ATCTTACCGC TGTGAGATC  
TCGTCTTGAA ATTTTCACGA GTAGTAACCT TTTGCAAGAA GCCCGGCTTT TGAGAGTTCC TAGAATGGCG ACAACTCTAG

---

9281 CAGTTCGATG TAACCCACTC GTGCACCCAA CTGATCTTCA GCATCTTTTA CTTTCACCAG CGTTTCTGGG TGAGCAAAAA  
GTCAAGCTAC ATTGGGTGAG CACGTGGGTT GACTAGAAGT CGTAGAAAAT GAAAGTGGTC GCAAAGACCC ACTCGTTTTT

---

9361 CAGGAAGGCA AAATGCCGCA AAAAAGGGAA TAAGGGCGAC ACGGAAATGT TGAATACTCA TACTCTTCTT TTTCAATAT  
GTCCTTCCGT TTTACGGCGT TTTTCCCTT ATTCCCGCTG TGCCTTTACA ACTTATGAGT ATGAGAAGGA AAAAGTTATA

---

9441 TATTGAAGCA TTTATCAGGG TTATTGTCTC ATGAGCGGAT ACATATTIGA ATGTATTTAG AAAAATAAAC AAATAGGGGT  
ATAACTTCGT AAATAGTCCC AATAACAGAG TACTCGCCTA TGTATAAACT TACATAAATC TTTTATTGT TTTATCCCCA

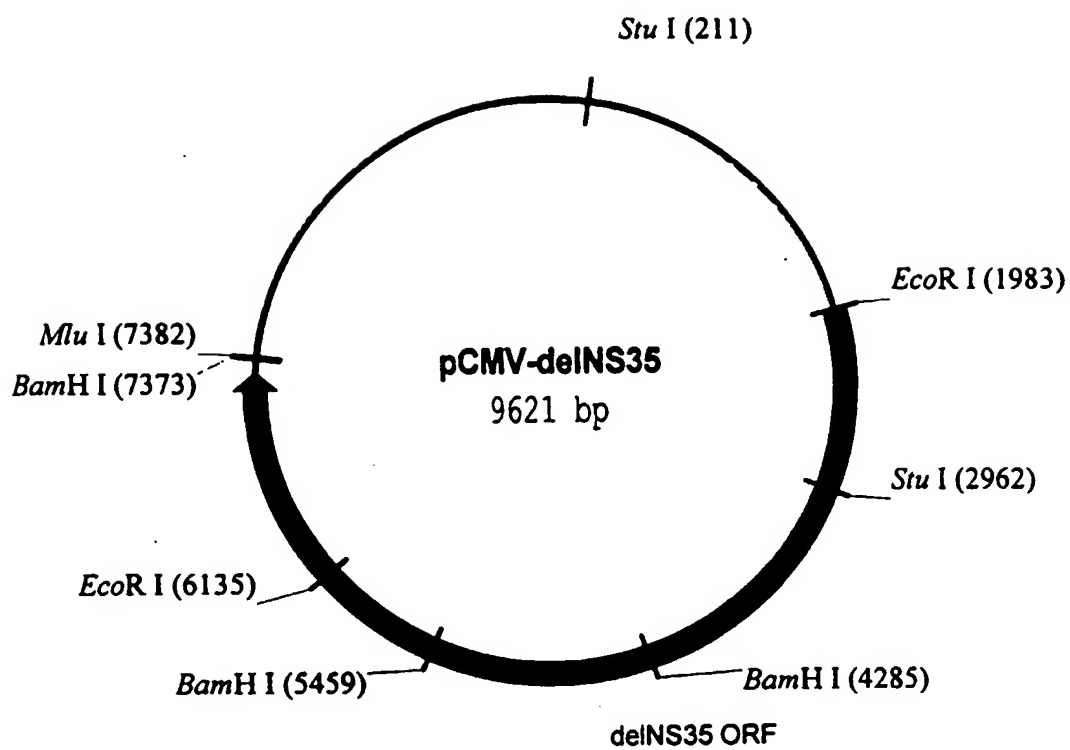
---

9521 TCCGCGCACA TTTCCCCGAA AAGTGCCACC TGACGTCTAA GAAACCATTA TTATCATGAC ATTAACCTAT AAAAATAGGC  
AGGCGCGTGT AAAGGGGCTT TTCACGGTGG ACTGCAGATT CTTTGTAAT AATAGTACTG TAATTGGATA TTTTATCCG

---

9601 GTATCAGGAG GCCCTTTCGT C  
CATAGTGCTC CGGGAAAGCA G

FIGURE 4



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## FIGURE 5 - Page 1

|      |            |            |            |            |            |            |            |             |
|------|------------|------------|------------|------------|------------|------------|------------|-------------|
| 1    | TCGCGCGTTT | CGGTGATGAC | GGTGAAAACC | TCTGACACAT | GCAGCTCCCG | GAGACGGTCA | CAGCTTGTCT | GTAAGCGGAT  |
|      | AGCGCGCAAA | GCCACTACTG | CCACTTTTGG | AGACTGTGTA | CGTCGAGGGC | CTCTGCCAGT | GTCGAACAGA | CATTCCGCCTA |
| 81   | GCCGGGAGCA | GACAAGCCCC | TCAGGGCGCG | TCAGCGGGTG | TTGGCGGGTG | TCGGGGCTGG | CTTAACATG  | CGGCATCAGA  |
|      | CGGCCCTCGT | CTGTTCCGGC | AGTCCCAGCG | AGTCGCCAC  | AACCGCCAC  | AGCCCCGACC | GAATTGATAC | GCCGTAGTCT  |
| StuI |            |            |            |            |            |            |            |             |
| 161  | GCAGATTGTA | CTGAGAGTGC | ACCATATGAA | GCTTTTTGCA | AAAGCCTAGG | CCTCCAAAAA | AGCCTCCTCA | CTACTTCTGG  |
|      | CGTCTAACAT | GACTCTCAGC | TGGTATACTT | CGAAAAACGT | TTTCGGATCC | GGAGGTTTTT | TCGGAGGAGT | GATGAAGACC  |
| 241  | AATAGCTCAG | AGGCCGAGGC | GGCCTCGGCC | TCTGCATAAA | TAAAAAAAT  | TAGTCAGCCA | TGGGGCGGAG | AATGGGCGGA  |
|      | TTATCGAGTC | TCCGGCTCCG | CCGGAGCCGG | AGACGTATTT | ATTTTTTTTA | ATCAGTCGGT | ACCCCGCCTC | TTACCCGCCT  |
| 321  | ACTGGGCGGG | GAGGGAATTA | TTGGCTATTG | GCCATCGCAT | ACGTTGTATC | TATATCATAA | TATGTACATT | TATATTGGCT  |
|      | TGACCCGCCC | CTCCCTTAAT | AACCGATAAC | CGGTAAACGT | TGCAACATAG | ATATAGTATT | ATACATGTAA | ATATAACCGA  |
| 401  | CATGTCCAAT | ATGACCGCCA | TGTGACATT  | GATTATTGAC | TAGTTATTAA | TAGTAATCAA | TTACGGGGTC | ATTAGTTTAT  |
|      | GTACAGGTTA | TACTGGCGGT | ACAACGTAA  | CTAATAACTG | ATCAATAATT | ATCATTAGTT | AATGCCCCAG | TAATCAAGTA  |
| 481  | AGCCCATATA | TGGAGTTCGG | CGTTACATAA | CTTACGGTAA | ATGGCCCGCC | TGGCTGACCG | CCCAACGACC | CCCGCCCAT   |
|      | TCGGGTATAT | ACCTCAAGGC | GCAATGTATT | GAATGCCATT | TACCGGGCGG | ACCGACTGGC | GGGTGTCTGG | GGGCGGGTAA  |
| 561  | GACGTCAATA | ATGACGTATG | TTCCCATAGT | AACGCCAATA | GGGACTTTCC | ATTGACGTCA | ATGGGTGGAG | TATTTACGGT  |
|      | CTGCAAGTAT | TACTGCATAC | AAGGGTATCA | TTGCGGTTAT | CCCTGAAAGG | TAACATGAGT | TACCCACCTC | ATAAATGCCA  |
| 641  | AAACTGCCCA | CTTGGCAGTA | CATCAAGTGT | ATCATATGCC | AAGTCCGCCC | CCTATTGACG | TCAATGACGG | TAAATGGCCC  |
|      | TTTGACGGGT | GAACCGTCAT | GTAGTTCACA | TAGTATACGG | TTCAGGCGGG | GGATAACTGC | AGTTACTGCC | ATTTACCGGG  |
| 721  | GCCTGGCATT | ATGCCAGTA  | CATGACCTTA | CGGGACTTTC | CTACTTGGCA | GTACATCTAC | GTATTAGTCA | TCGCTATTAC  |
|      | CGGACCGTAA | TACGGGTCAT | GTAATGGAAT | GCCCTGAAAG | GATGAACCGT | CATGTAGATG | CATAATCAGT | AGCGATAATG  |
| 801  | CATGGTGAIG | CGGTTTTGGC | AGTACACCAA | TGGGCGTGGA | TAGCGGTTTG | ACTCACGGGG | ATTTCCAAAT | CTCCACCCCA  |
|      | GTACCACTAC | GCCAAAACCG | TCATGTGGTT | ACCCGCACCT | ATCGCCAAAC | TGAGTGCCCC | TAAAGGTTCA | GAGGTGGGGT  |
| 881  | TTGACGTCAA | TGGGAGTTTG | TTTTGGCACC | AAAATCAACG | GGACTTTCCA | AAATGTCGTA | ATAACCCCGC | CCCGTTGACG  |
|      | AATGTCAGTT | ACCCTCAAAC | AAAACCGTGG | TTTATGTTGC | CCTGAAAGGT | TTTACAGCAT | TATTGGGGCG | GGGCAACTGC  |
| 961  | CAATGGGCG  | GTAGGCGTGT | ACGGTGGGAG | GTCTATATAA | GCAGAGCTCG | TTTAGTGAAC | CGTCAGATCG | CCTGGAGACG  |
|      | GTTTACCCGC | CATCCGCACA | TGCCACCCTC | CAGATATATT | CGTCTCGAGC | AAATCACTTG | GCAGTCTAGC | GGACCTCTGC  |
| 1041 | CCATCCACGC | TGTTTTGACC | TCCATAGAAG | ACACCGGGAC | CGATCCAGCC | TCCGCGGCGG | GGAACGGTGC | ATTGGAACGC  |
|      | GGTAGGTGCG | ACAAAACCTG | AGGTATCTTC | TGTGGCCCTG | GCTAGGTCGG | AGCGCGCCGC | CCTTGCCACG | TAACCTTGCG  |
| 1121 | GGATTCCCGG | TGCCAAGAGT | GACGTAAGTA | CCGCCTATAG | ACTCTATAGG | CACACCCCTT | TGGCTCTTAT | GCATGCTATA  |
|      | CCTAAGGGGC | ACGGTTCTCA | CTGCATTAT  | GGCGGATATC | TGAGATATCC | GTGTGGGGAA | ACCGAGAATA | CGTACGATAT  |
| 1201 | CTGTTTTTGG | CTTGGGGCCT | ATACACCCCC | GCTCCTTATG | CTATAGGTGA | TGGTATAGCT | TAGCCTATAG | GTGTGGGTAA  |
|      | GACAAAAACC | GAACCCCGGA | TATGTGGGGG | CGAGGAATAC | GATATCCACT | ACCATATCGA | ATCGGATATC | CACACCCAAT  |
| 1281 | TTGACCATTA | TTGACCACTC | CCCTATTGGT | GACGATACTT | TCCATTACTA | ATCCATAACA | TGGCTCTTTG | CCACAACAT   |
|      | AATGGTAAT  | AATGGTGAG  | GGGATAACCA | CTGCTATGAA | AGGTAATGAT | TAGGTATTGT | ACCGAGAAAC | GGTGTTGATA  |
| 1361 | CTCTATTGGC | TATATGCCAA | TACTCTGTCC | TTCAGAGACT | GACACGGACT | CTGTATTTTT | ACAGGATGGG | GTCCATTTAT  |
|      | GAGATAACCG | ATATACGGTT | ATGAGACAGG | AAGTCTCTGA | CTGTGCCTGA | GACATAAAAA | TGTCTTACCC | CAGGTAATAA  |

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## FIGURE 5 - Page 2

|      |             |             |            |             |            |            |            |            |  |
|------|-------------|-------------|------------|-------------|------------|------------|------------|------------|--|
| 1441 | TATTTACAAA  | TTCACATATA  | CAACAACGCC | GTCCCCCGTG  | CCCGCAGTTT | TTATTAAACA | TAGCGTGGGA | TCTCCGACAT |  |
|      | ATAAATGTTT  | AAGTGATAT   | GTGTTGCGG  | CAGGGGGCAC  | GGGCGTCAAA | AATAATTTGT | ATCGCACCT  | AGAGGCTGTA |  |
| 1521 | CTCGGTACG   | TGTTCCGGAC  | ATGGGCTCTT | CTCCGGTAGC  | GGCGGAGCTT | CCACATCCGA | GCCCTGGTCC | CATCCGTCCA |  |
|      | GAGCCCATGC  | ACAAGGCCCTG | TACCCGAGAA | GAGGCCATCG  | CCGCCTCGAA | GGTGTAGGCT | CGGGACCAGG | GTAGGCAGGT |  |
| 1601 | GCGGCTCATG  | GTCGCTCGGC  | AGTCCTTGC  | TCCTAACAGT  | GGAGGCCAGA | CTTAGGCACA | GCACAATGCC | CACCACCACC |  |
|      | CGCCGAGTAC  | CAGCGAGCCG  | TCGAGGAACG | AGGATTGTCA  | CCTCCGGTCT | GAATCCGTGT | CGTGTTACGG | GTGGTGGTGG |  |
| 1681 | AGTGTGCCGC  | ACAAGGCCGT  | GGCGGTAGGG | TATGTGTCTG  | AAAATGAGCT | CGGAGATTGG | GCTCGCACCT | GGACGCAGAT |  |
|      | TCACACGGCG  | TGTTCCGGCA  | CCGCCATCCC | ATACACAGAC  | TTTTACTCGA | GCCTCTAACC | CGAGCGTGGG | CCTGCGTCTA |  |
| 1761 | GGAAGACTTA  | AGGCAGCGGC  | AGAAGAAGAT | GCAGGCAGCT  | GAGTTGTGTG | ATTCTGATAA | GAGTCAGAGG | TAATCCCGT  |  |
|      | CCTTCTGAAT  | TCCGTCGCCG  | TCTTCTTCTA | CGTCCGTCGA  | CTCAACAACA | TAAGACTATT | CTCAGTCTCC | ATTGAGGGCA |  |
| 1841 | TGCGGTGCTG  | TTAACGGTGG  | AGGGCAGTGT | AGTCTGAGCA  | GTACTCGTTG | CTGCCGCGCG | CGCCACCAGA | CATAATAGCT |  |
|      | ACGCCACGAC  | AATTGCCACC  | TCCCGTCACA | TCAGACTCGT  | CATGAGCAAC | GACGGCGCGC | GCGGTGGTCT | GTATTATCGA |  |
| +2   |             |             |            |             |            |            | EcoRI      | M A A      |  |
| 1921 | GACAGACTAA  | CAGACTGTTT  | CTTTCCATGG | GTCITTTCTG  | CAGTCACCGT | CGTCGACCTA | AGAATTCACC | ATGGTGTCAT |  |
|      | CTGTCTGATT  | GTCTGACAAG  | GAAAGGTACC | CAGAAAAGAC  | GTCAGTGGCA | GCAGCTGGAT | TCTTAAGTGG | TACCGACGTA |  |
| +2   | Y A A Q     | G Y K       | V L V L    | N P S       | V A A      | T L G F    | G A Y      | M S K      |  |
| 2001 | ATGCAGCTCA  | GGGCTATAAG  | GTGCTAGTAC | TCAACCCCTC  | TGTTGCTGCA | ACACTGGGCT | TTGGTGCTTA | CATGTCCAAG |  |
|      | TACGTCGAGT  | CCCCTATATC  | CACGATCATG | AGTTGGGGAG  | ACAACGACGT | TGTGACCCGA | AACCACGAAT | GTACAGGTTC |  |
| +2   | A H G I     | D P N       | I R T      | G V R T     | I T T      | G S P      | I T Y S    | T Y G      |  |
| 2081 | GCTCATGGGA  | TCGATCCTAA  | CATCAGGACC | GGGGTGAGAA  | CAATTACCAC | TGGCAGCCCC | ATCACGTACT | CCACCTACGG |  |
|      | CGAGTACCCCT | AGCTAGGATT  | GTAGTCTCTG | CCCCACTCTT  | GTTAATGGTG | ACCGTCGGGG | TAGTGCATGA | GGTGGATGCC |  |
| +2   | K F L       | A D G G     | C S G      | G A Y       | D I I I    | C D E      | C H S      | T D A      |  |
| 2161 | CAAGTTCCTT  | GCCGACGGCG  | GGTGCTCGGG | GGGCGCTTAT  | GACATAATAA | TTTGTGACGA | GTGCCACTCC | ACGGATGCCA |  |
|      | GTTCAAGGAA  | CGGCTGCCGC  | CCACGAGCCC | CCCGCAATA   | CTGTATTATT | AAACACTGCT | CACGGTGAGG | TGCCTACGGT |  |
| +2   | T S I L     | G I G       | T V L D    | Q A E       | T A G      | A R L V    | V L A      | T A T      |  |
| 2241 | CATCCATCTT  | GGGCATTGGC  | ACTGTCTCTG | ACCAAGCAGA  | GACTGCGGGG | GCGAGACTGG | TTGTGCTCGC | CACCGCCACC |  |
|      | GTAGGTAGAA  | CCCGTAACCG  | TGACAGGAAC | TGGTTCGTCT  | CTGACGCCCC | CGCTCTGACC | AACACGAGCG | GTGGCGGTGG |  |
| +2   | P P G S     | V T V       | P H P      | N I E E     | V A L      | S T T      | G E I P    | F Y G      |  |
| 2321 | CCTCCGGGCT  | CCGTCACTGT  | GCCCCATCCC | AACATCGAGG  | AGGTGCTCT  | GTCCACCACC | GGAGAGATCC | CTTTTACGG  |  |
|      | GGAGGCCCGA  | GGCAGTGACA  | CGGGGTAGGG | TTGTAGCTCC  | TCCAACGAGA | CAGGTGGTGG | CCTCTCTAGG | GAAAAATGCC |  |
| +2   | K A I       | P L E V     | I K G      | G R H       | L I F C    | H S K      | K K C      | D E L      |  |
| 2401 | CAAGGCTATC  | CCCCTCGAAG  | TAATCAAGGG | GGGGAGACAT  | CTCATCTTCT | GTCATTCAAA | GAAGAAGTGC | GACGAACCTG |  |
|      | GTTCCGATAG  | GGGGAGCTTC  | ATTAGTTCCC | CCCCTCTGTA  | GAGTAGAAGA | CAGTAAGTTT | CTTCTTCACG | CTGCTTGAGC |  |
| +2   | A A K L     | V A L       | G I N A    | V A Y       | Y R G      | L D V S    | V I P      | T S G      |  |
| 2481 | CCGCAAAGCT  | GGTCGCATTG  | GGCATCAATG | CCGTGGCCTA  | CTACCGCGGT | CTTGACGTGT | CCGTATCCCC | GACCAGCGGC |  |
|      | GGCGTTTCCA  | CCAGCGTAAC  | CCGTAGTTAC | GGCACC GGAT | GATGGCGCCA | GAAGTGCACA | GGCAGTAGGG | CTGGTCGCCG |  |
| +2   | D V V V     | V A T       | D A L      | M T G Y     | T G D      | F D S      | V I D C    | N T C      |  |
| 2561 | GATGTTGTCG  | TCGTGGCAAC  | CGATGCCCTC | ATGACCGGCT  | ATACCGGCGA | CTTCGACTCG | GTGATAGACT | GCAATACGTG |  |
|      | CTACAACAGC  | AGCACCGTTG  | GCTACGGGAG | TACTGGCCGA  | TATGGCCGCT | GAAGCTGAGC | CACTATCTGA | CGTTATGCAC |  |



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## FIGURE 5 - Page 3

+2 V T Q T V D F S L D P T F T I E T I T L P Q D A V S  
 2641 TGTCACCCAG ACAGTCGATT TCAGCCTTGA CCTACCTTC ACCATTGAGA CAATCAGCT CCCCCAAGAT GCTGTCTCCC  
 ACAGTGGGTC TGTCAGCTAA AGTCGGAAC GGGATGGAAG TGGTAACTCT GTTAGTGCAG GGGGGTTCTA CGACAGAGGG

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+2 R T Q R R G R T G R G K P G I Y R F V A P G E R P S G  
 2721 GCACTCAACG TCGGGGCGAG ACTGGCAGGG GGAAGCCAGG CATCTACAGA TTTGTGGCAC CGGGGGAGCG CCCCTCCGGC  
 CGTGAGTTGC AGCCCCGTCC TGACCGTCCC CCTTCGGTCC GTAGATGTCT AAACACCGTG CCCCCTCGC GGGGAGSGCC

---

+2 M F D S S V L C E C Y D A G C A W Y E L T P A E T T V  
 2801 ATGTTCGACT CGTCCGTCTT CTGTGAGTGC TATGACGAG GCTGTGCTTG GTATGAGCTC ACGCCCGCCG AGACTACAGT  
 TACAAGCTGA GCAGGCAGGA GACACTCAGC ATACTGCGTC CGACACGAAC CATACTCGAG TGCGGGCGGC TCTGATGTCA

---

+2 R L R A Y M N T P G L P V C Q D H L E F W E G V F T  
 2881 TAGGCTACGA GCGTACATGA ACACCCCGGG GCTTCCCGTG TGCCAGGACC ATCTTGAATT TTGGGAGGGC GTCTTTACAG  
 ATCCGATGCT CGCATGTACT TGTGGGGCCC CGAAGGGCAC ACGGTCTGAG TAGAAGTTAA AACCTCCCG CAGAAATGTC

---

+2 G L T H I D A H F L S Q T K Q S G E N L P Y L V A Y Q  
 2961 GCCTCACTCA TATAGATGCC CACTTTCTAT CCCAGACAAA GCAGAGTGGG GAGAACCTTC CTTACCTGGT AGCGTACCAA  
 CGGAGTGAGT ATATCTACCG GTGAAAGATA GGGTCTGTTT CGTCTCACC CTCTTGAAG GAATGGACCA TCGATGGTT

---

+2 A T V C A R A Q A P P P S W D Q M W K C L I R L K P T  
 3041 GCCACCGTGT GCGCTAGGGC TCAAGCCCTT CCCCCTCATGT GGGACCATGT GTGGAAAGTGT TTGATTCGCC TCAAGCCAC  
 CGGTGGCACA CGCATCCCG AGTTCGGGGA GGGGGTAGCA CCTGTGCTA CACCTTACA AACTAAGCGG AGTTCGGGTG

---

+2 L H G P T P L L Y R L G A V Q N E I T L T H P V T K  
 3121 CCTCCATGGG CCAACACCCC TGCTATACAG ACTGGGCGCT GTTCAGAAATG AAATCACCCT GACGCACCCA GTCACCAAT  
 GGAGGTACCC GGTGTGGGG ACGATATGTC TGACCCCGCA CAAGTCTTAC TTTAGTGGGA TCGCGTGGT CAGTGGTTA

---

+2 Y I M T C M S A D L E V V T S T W V L V G G V L A A L  
 3201 ACATCATGAC ATGCATGTCG GCCGACCTGG AGGTCGTCAC GAGCACCTGG GTGCTCGTTG GCGGCGTCTT GGCTGCTTTG  
 TGTAGTACTG TACGTACAGC CGGCTGGACC TCCAGCAGTG CTCGTGGACC CACGAGCAAC CCGCGCAGGA CCGACGAAAC

---

+2 A A Y C L S T G C V V I V G R V V L S G K P A I I P D  
 3281 GCCGCGTATT GCCTGTCAAC AGGCTGCGTG GTCATAGTGG GCAGGGTCTT CTTGTCCGGG AAGCCGGCAA TCATACCTGA  
 CGCGGCATAA CGGACAGTTG TCCGACGCAC CAGTATCACC CGTCCCAGCA GAACAGGCC TCGGCGGCTT AGTATGGACT

---

+2 R E V L Y R E F D E M E E C S Q H L P Y I E Q G M M  
 3361 CAGGGAAGTC CTCTACCGAG AGTTCGATGA GATGGAAGAG TGCTCTCAGC ACTTACCGTA CATCGAGCAA GGGATGATGC  
 GTCCCTTCAG GAGATGGCTC TCAAGCTACT CTACCTTCTC ACGAGAGTCTG TGAATGGCAT GTAGCTCGTT CCCTACTACG

---

+2 L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V  
 3441 TCGCCGAGCA GTTCAAGCAG AAGGCCCTCG GCCTCTCTGCA GACCGCGTCC CGTCAGGCAG AGGTTATCGC CCCTGTGTG  
 AGCGGCTCGT CAAGTTCGTC TTCCGGGAGC CGGAGGACGT CTGGCGCAGG GCAGTCCGTC TCCAATAGCG GGGACGACAG

---

+2 Q T N W Q K L E T F W A K H M W N F I S G G I Q Y L A G  
 3521 CAGACCAACT GGCAAAAAC CGAGACCTTC TGGGCGAAGC ATATGTGGAA CTTATCAGT GGGATACAA CTGTGGCGGG  
 GTCTGGTTGA CCGTTTTTGA GCTCTGGAAG ACCCGCTTCT TATACACCTT GAAGTAGTCA CCCTATGTTA TGAACCGCCC

---

+2 L S T L P G N P A I A S L M A E T A A V T S P L T T  
 3601 CTTGTCAACG CTGCCTGGTA ACCCGCCCAT TGCTTCATTG ATGGCTTTTA CAGCTGCTGT CACCAGCCCA CTAACCACTA  
 GAACAGTTGC GACGGACCAT TGGGGCGGTA ACGAAGTAAC TACCGAAAT GTGACGACA GTGGTCGGGT GATTGGTGAT

---

+2 S Q T L L F N I L G G W V A A Q L A A P G A A T A F V  
 3681 GCCAAACCTT CCTCTTCAAC ATATTGGGGG GGTGGGTGGC TGCCAGCTC GCCGCCCGG GTGCCGCTAC TGCTTTGTG  
 CGGTTGGGA GGAGAAGTTG TATAACCCCC CCACCCACCG ACGGTCTGAG CGGCGGGGG CACGGCGATG ACGGAACAC

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FIGURE 5 - Page 4

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+2 G A G L A G A A I G. S V G L G K V L I D I L A G Y G A
3761. GGCCTGGCT TAGCTGGCG CGCCATCGGC AGTGTGGAC TGGGGAAGGT CCTCATAGAC ATCCTTGAG GGTATGGCG
CCGCACCGA ATCGACCGC GCGGTAGCCG TCACAACCTG ACCCTTCCA GGAGTATCTG TAGGAACGTC CCATACCGCG

+2 G V A G A L V A F K I M S G E V P S T E D L V N L L
3841 GGCCTGGCG GGAGCTCTTG TGGCATTCAA GATCATGAGC GGTGAGGTCC CCTCCACGGA GGACCTGGTC AATCTACTGC
CCGCACCGC CTCGAGAAC ACCGTAAGT CTAGTACTCG CCATCTCAGG GGAGGTGCCT CTGGACCG TTAGATGACC

+2 P A I L S P G A L V V G V V C A A I L R R H V G P G E
3921 CCGCATCCT CTCGCCCGA GCCCTCGTAG TCGGCGTGGT CTGTGCAGCA ATACTGCGCC GGCACGTTGG CCCGGGCGAG
GGCGGTAGGA GAGCGGGCCT CGGGAGCATC AGCCGACCA GACACGTCGT TATGACGCGG CCGTGAAC GGGCCGCTC

+2 G A V Q W M N R L I A F A S R G N H V S P T H Y V P E
4001 GGGCAGTGC AGTGGATGAA CCGGCTGATA GCCTTCGCCT CCCGGGGGAA CCATGTTTCC CCCACGCACT ACCTGCCGGA
CCCCGTCACG TCACCTACTT GGCCGACTAT CGGAAGCGGA GGGCCCCCTT GGTACAAAG GGGTGCCTGA TGCACGGCTC

+2 S D A A A R V T A I L S S L T V T Q L L R R L H Q W
4081 GAGCGATGCA GCTGCCCGC TCACTGCCAT ACTCAGCAGC CTCAGTGTAA CCCAGCTCCT GAGGCGACTG CACGAGTGA
CTCGCTACGT CGACGGGCGC AGTGACGGTA TGAGTCGTCG GAGTGACATT GGTGCGAGGA CTCGCTGAC GTGTCACCT

+2 I S S E C T T P C S G S W L R D I W D W I C E V L S D
4161 TAAGCTCGGA GTGTACCACT CCATGCTCCG GTTCTGGCT AAGGGACATC TGGGACTGGA TATGCGAGGT GTTGAGCGAC
ATTGAGCCT CACATGGTGA GGTACGAGG CAAGGACCGA TTCCCTGTAG ACCCTGACCT ATACGCTCCA CAACTCGCTG

+2 F K T W L K A K L M P Q L P G I P F V S C Q R G Y K G
BamHI
4241 TTTAAGACCT GGCTAAAAGC TAAGCTCATG CCACAGTGC CTGGGATCCC CTTGTGTGCC TGCCAGCGCG GGTATAAGGG
AAATTCTGGA CCGATTTTCG ATTCGAGTAC GGTGTCGACG GACCCTAGGG GAAACACAGG ACGGTCGCGC CCATATTCCC

+2 V W R G D G I M H T R C H C G A E I T G H V K N G T
4321 GGTCTGGCGA GGGGACGGCA TCATGCACAC TCGCTGCCAC TGTGGAGCTG AGATCACTGG ACATGTCAA AACGGGCGA
CGAGACCGCT CCCCTGCCGT AGTACGTGTG AGCGACGGTG ACACCTCGAC TCTAGTGACC TGTACAGTTT TTGCCCTGCT

+2 M R I V G P R T C R N M W S G T F P I N A Y T T G P C
4401 TGAGGATCGT CGGTCCTAGG ACCTGCAGGA ACATGTGGAG TGGGACCTTC CCATTAATG CCTACACCAC GGGCCCCGTG
ACTCCTAGCA GCCAGGATCC TGGACGTCT TGTACACCTC ACCCTGGAAG GGGTAATTAC GGATGTGGTG CCCGGGGACA

+2 T P L P A P N Y T F A L W R V S A E E Y V E I R Q V G
4481 ACCCCCCTTC CTGCGCCGAA CTACACGTTG GCGCTATGGA GGGTGTCTGC AGAGGAATAC GTGGAGATAA GGCAGGTGGG
TGGGGGGAAG GACGCGGCTT GATGTGCAAG CGCGATACCT CCCACAGAGC TCTCCTTATG CACCTCTATT CCGTCCACCC

+2 D F H Y V T G M T T D N L K C P C Q V P S P E F F T
4561 GGACTTCCAC TACGTGACGG GTATGACTAC TGACAATCTT AAATGCCCCG GCCAGGTCCC ATCGCCCGAA TTTTTCACAG
CCTGAAGGTG ATGCACTGCC CATACTGATG ACTGTTAGAA TTTACGGGCA CGGTCCAGGG TAGCGGGCTT AAAAAGTGTC

+2 E L D G V R L H R F A P P C K P L L R E E V S F R V G
4641 AATTGGACGG GGTGCGCCTA CATAGGTTTG CGCCCCCTG CAAGCCCTTG CTGCGGGAGG AGGTATCATT CAGAGTAGGA
TTAACCTGCC CCACGCGGAT GTATCCAAAC GCGGGGGGAC GTTCGGGAAC GACGCCCTCC TCCATAGTAA GTCTCATCT

+2 L H E Y P V G S O L P C E P E P D V A V L T S M L T D
4721 CTCCACGAAT ACCCGGTAGG GTCGCAATTA CTTTGCAGC CCGAACCGGA CGTGGCCGTG TTGACGTCCA TGCTCACTGA
GAGGTGCTTA TGGGCCATCC CAGCGTTAAT GGAACGCTCG GGCTTGGCCT GCACCGGCAC AACTGCAGGT ACGAGTACT

+2 P S H I T A E A A G R R L A R G S P P S V A S S S A
4801 TCCTCCCAT ATAACAGCAG AGGCGGCCG GCGAAGGTTG GCGAGGGGAT CACCCCCCTC TGTGGCCAGC TCCTCGGCTA
AGGAGGGGTA TATTGTCGTC TCCGCGGGC CGCTTCCAAC CGCTCCCTA GTGGGGGGAG ACACCGGTG AGGAGCCGAT

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|      |            |            |            |            |            |             |            |            |            |            |            |            |             |             |             |            |   |   |   |   |   |   |   |   |   |   |   |
|------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|-------------|-------------|-------------|------------|---|---|---|---|---|---|---|---|---|---|---|
| +2   | S          | Q          | L          | S          | A          | P           | S          | L          | K          | A          | T          | C          | T           | A           | N           | H          | D | S | P | D | A | E | L | I | E | A | N |
| 4881 | GCCAGCTATC | CGCTCCATCT | CTCAAGGCAA | CTTGACCCGC | TAACCATGAC | TCCCCTGATG  | CTGAGCTCAT | AGAGGCCAAC | CGGTGATAG  | GCGAGGTAGA | GAGTCCGTT  | GAACGTGGCG | ATTGGTACTG  | AGGGGACTAC  | GACTCGAGTA  | TCTCCGGTTG |   |   |   |   |   |   |   |   |   |   |   |
| +2   | L          | L          | W          | R          | Q          | E           | M          | G          | G          | N          | I          | T          | R           | V           | E           | S          | E | N | K | V | V | I | L | D | S | F | D |
| 4961 | CTCTATGGA  | GGCAGGAGAT | GGGCGGCAAC | ATCACCAGGG | TTGAGTCAGA | AAACAAAGTG  | GTGATTCTGG | ACTCCTTCGA | GAGGATACCT | CCGTCTCTTA | CCCGCCGTTG | TAGTGGTCCC | AACCTCAGTCT | TTTGTITTCAC | CACCTAAGACC | TGAGGAAGCT |   |   |   |   |   |   |   |   |   |   |   |
| +2   | P          | L          | V          | A          | E          | E           | D          | E          | R          | E          | I          | S          | V           | P           | A           | E          | I | L | R | K | S | R | R | F | A | Q |   |
| 5041 | TCCGCTTGTG | GCGGAGGAGG | ACGAGCGGGA | GATCTCCGTA | CCCGCAGAAA | TCCCTGCGGAA | GTCTCGGAGA | TTCGCCCAGG | AGGGGAACAC | CGCTCTCTCC | TGCTCGCCCT | CTAGAGGCAT | GGGCGTCTTT  | AGGACGCCCT  | CAGAGCCTCT  | AAGCGGGTCC |   |   |   |   |   |   |   |   |   |   |   |
| +2   | A          | L          | P          | V          | W          | A           | R          | P          | D          | Y          | N          | P          | P           | L           | V           | E          | T | W | K | K | P | D | Y | E | P | P | V |
| 5121 | CCCTGCCCGT | TGGGGCGCGG | CCGACTATA  | ACCCCCCGCT | AGTGGAGACG | TGGAAAAGC   | CCGACTACGA | ACCACCTGTG | GGGACGGGCA | AACCCGCGCC | GGCCTGATAT | TGGGGGGCGA | TCACCTCTGC  | ACCTTTTTCG  | GGCTGATGCT  | TGGTGACAC  |   |   |   |   |   |   |   |   |   |   |   |
| +2   | V          | H          | G          | C          | P          | L           | P          | P          | P          | K          | S          | P          | P           | V           | P           | P          | P | R | K | K | R | T | V | V | L | T | E |
| 5201 | GTCCATGSGT | GCCCGTCTCC | ACCTCCAAAG | TCCCTCCTG  | TGCTCCGCG  | TGGGAAGAAG  | CGGACGGTGG | TCTCTACTGA | CAGGTACCGA | CGGGCGAAGG | TGGAGGTTTC | AGGGGAGGAC | ACGGAGGCGG  | AGCCTTCTTC  | GCCTGCCACC  | AGGAGTGACT |   |   |   |   |   |   |   |   |   |   |   |
| +2   | S          | T          | L          | S          | T          | A           | L          | A          | E          | L          | A          | T          | R           | S           | F           | G          | S | S | S | T | S | G | I | T | G | D |   |
| 5281 | ATCAACCCTA | TCTACTGCCT | TGGCCGAGCT | CGCCACCAGA | AGCTTTGGCA | GCTCCTCAAC  | TTCCGGCATT | ACGGGCGACA | TAGTTGGGAT | AGATGACGGA | ACCGGCTCGA | GCGGTGGTCT | TCGAAACCGT  | CGAGGAGTTG  | AAGGCCGTAA  | TGCCCGCTGT |   |   |   |   |   |   |   |   |   |   |   |
| +2   | N          | T          | T          | T          | S          | S           | E          | P          | A          | P          | S          | G          | C           | P           | P           | D          | S | D | A | E | S | Y | S | S | M | P | P |
| 5361 | ATACGACAAC | ATCCTCTGAG | CCCGCCCCCT | CTGGCTGCC  | CCCCGACTCC | GACGCTGAGT  | CCTATTCTCT | CATGCCCCC  | TATGCTGTTG | TAGGAGACTC | GGGCGGGGAA | GACCGACGGG | GGGGCTGAGG  | CTGCGACTCA  | GGATAAGGAG  | GTACGGGGGG |   |   |   |   |   |   |   |   |   |   |   |
| +2   | L          | E          | G          | E          | P          | G           | D          | P          | D          | L          | S          | D          | G           | S           | W           | S          | T | V | S | S | E | A | N | A | E | D | V |
|      |            |            |            |            |            |             |            |            |            |            |            |            |             |             |             |            |   |   |   |   |   |   |   |   |   |   |   |
| 5441 | CTGGAGGGGG | AGCCTGGGGA | TCCGGATCTT | AGCGACGGGT | CATGGTCAAC | GGTCAGTAGT  | GAGGCCAACG | CGGAGGATGT | GACCTCCCCC | TCGGACCCCT | AGGCCTAGAA | TCGCTGCCCA | GTACCACTTG  | CCAGTCATCA  | CTCCGGTTGC  | GCCTCCTACA |   |   |   |   |   |   |   |   |   |   |   |
| +2   | V          | C          | C          | S          | M          | S           | Y          | S          | W          | T          | G          | A          | L           | V           | T           | P          | C | A | A | E | E | Q | K | L | P | I |   |
| 5521 | CGTGTGCTGC | TCAATGTCTT | ACTCTTGGAC | AGGCGCACTC | GTACCCCGGT | GCGCCGCGGA  | AGAACAGAAA | CTGCCCATCA | GCACACGACG | AGTTACAGAA | TGAGAACCTG | TCCGCTGTAG | CAGTGGGGCA  | CGCGGCGCCT  | TCTGTCTTT   | GACGGGTAGT |   |   |   |   |   |   |   |   |   |   |   |
| +2   | N          | A          | L          | S          | N          | S           | L          | L          | R          | H          | H          | N          | L           | V           | Y           | S          | T | T | S | R | S | A | C | O | R | Q | K |
| 5601 | ATGCACTAAG | CAACTCGTTG | CTAGCTCACC | ACAATTTGGT | GTATTCCACC | ACCTCAGCGA  | GTGCTTGCCA | AAGGCAGAAG | TACGTGATTC | GTTGAGCAAC | GATGCAGTGG | TGTTAAACCA | CATAAGGTGG  | TGGAGTGCGT  | CACGAACGGT  | TTCCGTCTTC |   |   |   |   |   |   |   |   |   |   |   |
| +2   | K          | V          | T          | F          | D          | R           | L          | Q          | V          | L          | D          | S          | H           | Y           | Q           | D          | V | L | K | E | V | K | A | A | A | S | K |
| 5681 | AAAGTCACAT | TTGACAGACT | GCAAGTTCTG | GACAGCCATT | ACCAGGACGT | ACTCAAGGAG  | GTAAAGCAG  | CGGCGTCAAA | TTTCAGTGTA | AACTGTCTGA | CGTTCAAGAC | CTGTCCGTAA | TGGTCTCTGA  | TGAGTTCCTC  | CAATTTCTGC  | GCCGCACTTT |   |   |   |   |   |   |   |   |   |   |   |
| +2   | V          | K          | A          | N          | L          | L           | S          | V          | E          | E          | A          | C          | S           | L           | T           | P          | P | H | S | A | K | S | K | F | G | Y |   |
| 5761 | AGTGAAGGCT | AACCTGCTAT | CCGTAGAGGA | AGCTTGACGC | CTGACGCCCC | CACACTCAGC  | CAAATCCAAG | TTTGGTTATG | TCACTTCCGA | TTGAACGATA | GGCATCTCCT | TCGAACGTGC | GACTGCGGGG  | GTGTGAGTCG  | GTTTAGGTTT  | AAACCAATAC |   |   |   |   |   |   |   |   |   |   |   |
| +2   | G          | A          | K          | D          | V          | R           | C          | H          | A          | R          | K          | A          | V           | T           | H           | I          | N | S | V | W | K | D | L | L | E | D | N |
| 5841 | GGGCAAAAGA | CGTCCGTTGC | CATGCCAGAA | AGGCCGTAA  | CCACATCAAC | TCCGTGTGGA  | AAGACCTTCT | GGAAGACAAT | CCCGTTTCT  | GCAGGCAACG | GTACGGTCTT | TCCGGCATTG | GGTGTAGTTG  | AGGCACACCT  | TTCTGGAAGA  | CCTTCTGTTA |   |   |   |   |   |   |   |   |   |   |   |
| +2   | V          | T          | P          | I          | D          | T           | T          | I          | M          | A          | K          | N          | E           | V           | F           | C          | V | Q | P | E | K | G | G | R | K | P | A |
| 5921 | GTAACACCAA | TAGACACTAC | CATCATGGCT | AAGAACGAGG | TTTTCTGCGT | TCAGCCTGAG  | AAGGGGGGTC | GTAAGCCAGC | CATTGTGGTT | ATCTGTGATG | GTAGTACCGA | TTCTTGCTCC | AAAAGACGCA  | AGTCGGACTC  | TTCCCCCAG   | CATTCCGTCG |   |   |   |   |   |   |   |   |   |   |   |

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FIGURE 5 - Page 6

+2 R L I V F P D L G V R V C E K M A L Y D V V T K L P  
 6001 TCGTCTCATC GTGTTCCCG ATCTGGGCGT GCGCGTGTGC GAAAGATGG CTTTGTACGA CGTGGTTACA AAGTCCCCT  
 AGCAGAGTAG CACAAGGGG TAGACCCGCA CGCGCACACG CTTTCTACC GAAACATGCT GCACCAATGT TTCGAGGGGA  
 +2 L A V M G S S Y G F Q Y S P G Q R V E F L V Q A W K S  
 EcoRI  
 6081 TGGCCGTGAT GGGAAGCTCC TACGGATTCC AATACTCACC AGGACAGCGG GTTGAATTCC TCGTGCAAGC GTGGAAGTCC  
 ACGGGCACTA CCCTTCGAGG ATGCCTAAGG TTATGAGTGG TCCTGTGCGC CAACTTAAGG AGCACGTTCC CACCTTCAGG  
 +2 K K T P M G F S Y D T R C F D S T V T E S D I R T E E  
 6161 AAGAAAACCC CAATGGGGTT CTCGTATGAT ACCCGCTGCT TTGACTCCAC AGTCACTGAG AGCGACATCC GTACGGAGGA  
 TTCTTTTGGG GTTACCCCAA GAGCATACTA TGGGCGACGA AACTGAGGTG TCAGTGACTC TCGCTGTAGG CATGCCTCT  
 +2 A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G  
 6241 GGCAATCTAC CAATGTTGTG ACCTCGACCC CCAAGCCCGC GTGGCCATCA AGTCCCTCAC CGAGAGGCTT TATGTTGGGG  
 CCGTTAGATG GTTACAACAC TGGAGCTGGG GGTTCGGGCG CACCGGTAGT TCAGGGAGTG GCTCTCCGAA ATACAACCC  
 +2 G P L T N S R G E N C G Y R R C R A S G V L T T S C G  
 6321 GCCCTCTTAC CAATCAAGG GGGGAGAACT GCGGCTATCG CAGGTGCCGC GCGAGCGGCG TACTGACAAC TAGCTGTGGT  
 CGGGAGAATG GTTAAGTTCC CCCCTCTTGA CGCCGATAGC GTCCACGGCG CGCTCGCCGC ATGACTGTTG ATCGACACCA  
 +2 N T L T C Y I K A R A A C R A A G L Q D C T M L V C G  
 6401 AACACCCTCA CTTGCTACAT CAAGGCCCGG GCAGGCTGTC GAGCCGACAG GCTCCAGGAC TGCACCATGC TCGTGTGTGG  
 TTGTGGGAGT GAACGATGTA GTTCCGGGCC CGTCGGACAG CTCGGCGTCC CGAGGTCCTG ACGTGGTACG AGCACACACC  
 +2 D J L V V I C E S A G V Q E D A A S L R A F T E A M  
 6481 CGACGACTTA GTCGTTATCT GTGAAAGCGC GGGGGTCCAG GAGGACGCGG CGAGCCTGAG AGCCTTACG GAGGGTATGA  
 GTGCTGAAT CAGCAATAGA CACTTTCGCG CCCCAGGTC CTCTGCGCC GCTCGGACTC TCGGAAGTGC CTCGATACT  
 +2 T R Y S A P P G D P P Q P E Y D L E L I T S C S S N V  
 6561 CCAGGTACTC CGCCCCCCT GGGGACCCCG CACAACCAGA ATACGACTTG GAGCTCATAA CATCATGCTC CTCCAACGTG  
 GGTCATGAG GCGGGGGGGA CCCCTGGGGG GTGTGGTCT TATGCTGAAC CTCGAGTATT GTAGTAGCAG GAGGTGAC  
 +2 S V A H D G A G K R V Y Y L T R D P T T P L A R A A W  
 6641 TCAGTCGCCC ACGACGGCGC TGGAAAGAGG GTCTACTACC TCACCCGTGA CCCTACAACC CCCCTCGCGA GAGGTGCGTG  
 AGTCAGCGGG TGCTGCCGCG ACCTTCTCC CAGATGATGG AGTGGGCACT GGGATGTTGG GGGGAGCGCT CTCGACGCAC  
 +2 E T A R H T P V N S W L G N I I M F A P T L W A R M  
 6721 GGAGACAGCA AGACACACTC CAGTCAATTC CTGGCTAGGC AACATAATCA TGTTTGCCCC CAACTGTGG GCGAGGATGA  
 CCTCTGTCGT TCTGTGTGAG GTCAGTTAAG GACCGATCCG TTGTATTAGT ACAAACGGGG GTGTGACACC CGCTCCTACT  
 +2 I L M T H F F S V L I A R D Q L E Q A L D C E I Y G A  
 6801 TACTGATGAC CCATTCTTT AGCGTCCCTA TAGCCAGGGA CCAGCTTGAA CAGGCCCTCG ATTGCGAGAT CTACGGGGCC  
 ATGACTACTG GGTAAAGAAA TCGCAGGAAT ATCGGTCCCT GGTGAACTT GTCCGGGAGC TAACGCTCTA GATGCCCCG  
 +2 C Y S I E P L D L P P I I Q R L H G L S A F S L H S Y  
 6881 TGCTACTCCA TAGAACCCTT GGATCTACCT CCAATCATTC AAAGACTCCA TGGCCTCAGC GCATTTTTCAC TCCACAGTTA  
 ACGATGAGGT ATCTTGGTGA CCTAGATGGA GGTAGTAGG TTTCTGAGGT ACCGGAGTCG CGTAAAGTG AGGTGTCAAT  
 +2 S P G E I N R V A A C L R K L G V P P L R A W R H R  
 6961 CTCTCCAGGT GAAATCAATA GGGTGGCCGC ATGCCTCAGA AAAGTTGGGG TACCGCCCTT GCGAGCTTGG AGACACGGGG  
 GAGAGGTCCA CTTTAGTTAT CCCACGGCG TACGGAGTCT TTTGAACCC ATGGCGGGAA CGCTCGAACC TCTGTGGCCC  
 +2 A R S V R A R L L A R G G R A A I C G K Y L F N W A V  
 7041 CCGGAGCGT CCGCGCTAGG CTTCTGGCCA GAGGAGGCG GGCTGCCATA TGTGGCAAGT ACCTCTTCAA CTGGGCGAGT  
 GGGCCTCGCA GGCGCGATCC GAAGACCGGT CTCCTCCGTC CCGACGGTAT ACACCGTTCA TGGAGAGTT GACCCGTCAT

**FIGURE 5 - Page 7**

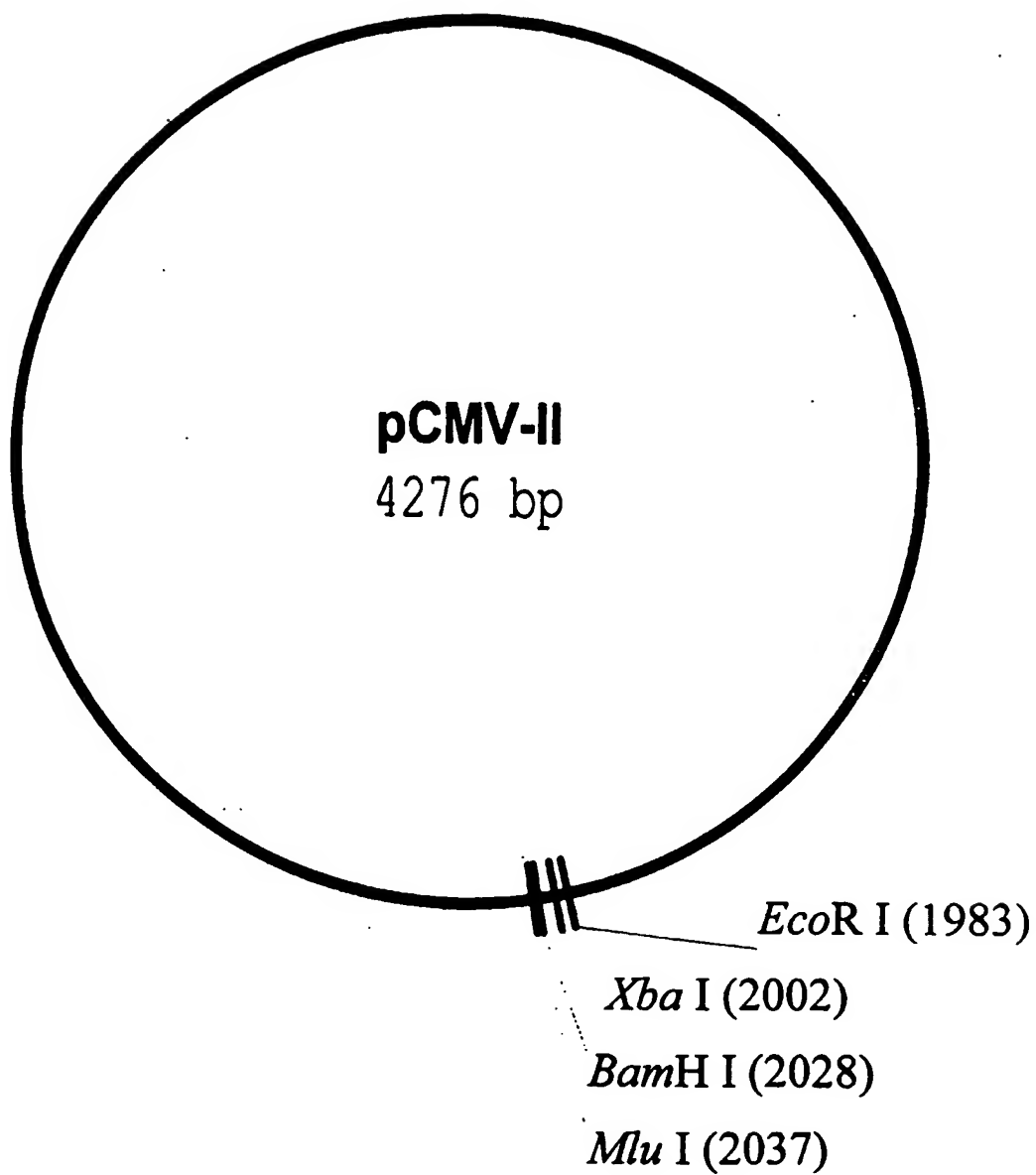
18/100

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## FIGURE 5 - Page 8

|      |             |            |            |             |             |             |            |             |
|------|-------------|------------|------------|-------------|-------------|-------------|------------|-------------|
| 8481 | ATCTTACCT   | AGATCCTTTT | AAATTAAAA  | TGAAGTTT    | AATCAATCTA  | AAGTATATAT  | GAGTAACTT  | GGTCTGACAG  |
|      | TAGAAGTGA   | TCTAGGAAA  | TITAATTTT  | ACTTCAAAAT  | TAGTTAGAT   | TTCATATATA  | CTCATTGAA  | CCAGACTGTC  |
| 8561 | TTACCAATGC  | TTAATCAGTG | AGGCACCTAT | CTCAGCGATC  | TGTCTATTTT  | GTTTCATCCAT | AGTTGCCTGA | CTCCCGCTCG  |
|      | AATGGTTACG  | AATTAGTCAC | TCCGTGGATA | GAGTCGCTAG  | ACAGATAAAG  | CAAGTAGGTA  | TCAACGGACT | GAGGGGCAGC  |
| 8641 | TGTAGATAAC  | TACGATACGG | GAGGGCTTAC | CATCTGGCCC  | CAGTGTCTGCA | ATGATACCGC  | GAGACCCACG | CTCACC GGCT |
|      | ACATCTATTG  | ATGCTATGCC | CTCCCGAATG | GTAGACCGGG  | GTCACGACGT  | TACTATGGCG  | CTCTGGGTGC | GAGTGGCCGA  |
| 8721 | CCAGATTTAT  | CAGCAATAAA | CCAGCCAGCC | GGAAGGGCCG  | AGCGCAGAAG  | TGGTCCTGCA  | ACTTTATCCG | CCTCCATCCA  |
|      | GGTCTAAATA  | GTCGTTATTT | GGTCGGTCGG | CCTTCCCGGC  | TCGCGCTTTC  | ACCAGGACGT  | TGAAATAGGC | GGAGGTAGGT  |
| 8801 | GTCTATTAA   | TGTTGCCGGG | AAGCTAGAGT | AAGTAGTTTC  | CCAGTTAATA  | GTTTGCGCAA  | CGTTGTTGCC | ATTGCTACAG  |
|      | CAGATAATTA  | ACAACGGCCC | TTCGATCTCA | TTCATCAAGC  | GGTCAATTAT  | CAAACGCGTT  | GCAACAACCG | TAACGATGTC  |
| 8881 | GCATCGTGGT  | GTCACGCTCG | TCGTTTGGTA | TGGCTTCATT  | CAGCTCCGGT  | TCCCAACGAT  | CAAGGCGAGT | TACATGATCC  |
|      | CGTAGCACCA  | CAGTGCAGC  | AGCAAACCAT | ACCGAAGTAA  | GTCGAGGCCA  | AGGGTTGCTA  | GTTCCGCTCA | ATGTACTAGG  |
| 8961 | CCCATGTTGT  | GCAAAAAAGC | GGTTAGCTCC | TTCGGTCTCT  | CGATCGTTGT  | CAGAAGTAAG  | TTGGCCGCG  | TGTTATCACT  |
|      | GGGTACAACA  | CGTTTTTTCG | CCAATCGAGG | AAGCCAGGAG  | GCTAGCAACA  | GTCTTCATT   | AACCGGCGTC | ACAATAGTGA  |
| 9041 | CATGTTTATG  | GCAGCACTGC | ATAATTCTCT | TACTGTCTATG | CCATCCGTAA  | GATGCTTTTC  | TGTGACTGGT | GAGTACTCAA  |
|      | GTACCAATAC  | CGTCGTGACG | TATTAAGAGA | ATGACAGTAC  | GGTAGGCATT  | CTACGAAAAG  | ACACTGACCA | CTCATGAGTT  |
| 9121 | CCAAGTCATT  | CTGAGAATAG | TGTATGCGGC | GACCGAGTTG  | CTCTTGCCCG  | GCGTCAATAC  | GGGATAATAC | CGCGCCACAT  |
|      | GGTTCAGTAA  | GACTCTTATC | ACATACGCCG | CTGGCTCAAC  | GAGAACGGGC  | CGCAGTTATG  | CCCTATTATG | GCGCGGTGTA  |
| 9201 | AGCAGAAGCTT | TAAAAGTGCT | CATCATTGGA | AAACGTTCTT  | CGGGGCGAAA  | ACTCTCAAGG  | ATCTTACCGC | TGTTGAGATC  |
|      | TCGTCTTGAA  | ATTTTCACGA | GTAGTAACCT | TTTGCAAGAA  | GCCCCGCTTT  | TGAGAGTTCC  | TAGAATGGCG | ACAACCTCTAG |
| 9281 | CAGTTTCGATG | TAACCCACTC | GTGCACCCAA | CTGATCTTCA  | GCATCTTTTA  | CTTTCACCAG  | CGTTTCTGGG | TGAGCAAAAA  |
|      | GTCAAGCTAC  | ATTGGGTGAG | CACGTGGGTT | GACTAGAAGT  | CGTAGAAAAT  | GAAAGTGGTC  | GCAAAGACCC | ACTCGTTTTT  |
| 9361 | CAGGAAGGCA  | AAATGCCGCA | AAAAAGGGAA | TAAGGGCGAC  | ACGGAATGT   | TGAATACTCA  | TACTCTTCCT | TTTTCAATAT  |
|      | GTCTTCCGT   | TTTACGGCGT | TTTTTCCCTT | ATTCGCCGTG  | TGCCTTTACA  | ACTTATGAGT  | ATGAGAAGGA | AAAAGTTATA  |
| 9441 | TATTGAAGCA  | TTTATCAGGG | TTATTGTCTC | ATGAGCGGAT  | ACATATTTGA  | ATGTATTTAG  | AAAAATAAAC | AAATAGGGGT  |
|      | ATAACTTCGT  | AAATAGTCCC | AATAACAGAG | TACTCGCCTA  | TGTATAAACT  | TACATAAATC  | TTTTTATTTG | TTTATCCCCA  |
| 9521 | TCCGCGCACA  | TTTCCCCGAA | AAGTGCCACC | TGACGTCTAA  | GAAACCATT   | TTATCATGAC  | ATTAACCTAT | AAAAATAGGC  |
|      | AGGCGCGTGT  | AAAGGGGCTT | TTCACGGTGG | ACTGCAGATT  | CTTTGGTAAT  | AATAGTACTG  | TAATTGGATA | TTTTTATCCG  |
| 9601 | GTATCACGAG  | GCCCTTTCGT | C          |             |             |             |            |             |
|      | CATAGTGCTC  | CGGAAAGCA  | G          |             |             |             |            |             |

**FIGURE 6**



## pCMV-II

FIGURE 7 - Page 1

|      |             |             |             |            |            |            |             |             |
|------|-------------|-------------|-------------|------------|------------|------------|-------------|-------------|
| 1    | TCGCGCGTTT  | CGGTGATGAC  | GGTGAAAACC  | TCTGACACAT | GCAGCTCCCG | GAGACGGTCA | CAGCTTGTCT  | GTAAGCGGAT  |
|      | AGCGCGCAAA  | GCCACTACTG  | CCACTTTTGG  | AGACTGTGTA | CGTCGAGGGC | CTCTGCCAGT | GTCGAACAGA  | CATTCCGCTA  |
| 81   | GCCGGGAGCA  | GACAAGCCCG  | TCAGGGCGCG  | TCAGCGGGTG | TTGGCGGGTG | TCGGGGCTGG | CTTAAGTATG  | CGGCATCAGA  |
|      | CGGCCCTCGT  | CTGTTCCGGC  | AGTCCCGCGC  | AGTCGCCAC  | AACCGCCAC  | AGCCCGGACC | GAATTGATAC  | GCCGTAGTCT  |
| 161  | GCAGATTGTA  | CTGAGAGTGC  | ACCATATGAA  | GCTTTTGTGA | AAAGCCTAGG | CCTCCAAAAA | AGCCTCTCA   | CTACTTCTGG  |
|      | CGTCTAACAT  | GACTCTCAG   | TGGTATACTT  | CGAAAAACGT | TTTCGGATCC | GGAGGTTTTT | TCGGAGGAGT  | GATGAAGACC  |
| 241  | AATAGCTCAG  | AGGCCGAGGC  | GGCCTCGGCC  | TCTGCATAAA | TAAAAAAAT  | TAGTCAGCCA | TGGGGCGGAG  | AATGGGCGGA  |
|      | TTATCGAGTC  | TCCGGCTCCG  | CCGGAGCCGG  | AGACGTATTT | ATTTTTTTTA | ATCAGTCGGT | ACCCCGCCTC  | TTACCCGCCCT |
| 321  | ACTGGGCGGG  | GAGGGAATTA  | TTGGCTATTG  | GCCATTGCAT | ACGTTGTATC | TATATCATAA | TATGTACATT  | TATATTGGCT  |
|      | TGACCCGCC   | CTCCCTTAAT  | AACCGATAAC  | CGGTAACGTA | TGCAACATAG | ATATAGTATT | ATACATGTAA  | ATATAACCGA  |
| 401  | CATGTCCAAT  | ATGACCGCCA  | TGTTGACATT  | GATTATTGAC | TAGTTATTAA | TAGTAATCAA | TTACGGGGTC  | ATTAGTTCAT  |
|      | GTACAGGTTA  | TACTGGCGGT  | ACAACGTAA   | CTAATAACTG | ATCAATAATT | ATCATTAGTT | AATGCCCCAG  | TAATCAAGTA  |
| 481  | AGCCCATATA  | TGGAGTCCG   | CGTTACATAA  | CTTACGGTAA | ATGGCCCGCC | TGGCTGACCG | CCCAACGACC  | CCCGCCCAT   |
|      | TCGGGTATAT  | ACCTCAAGGC  | GCAATGTATT  | GAATGCCATT | TACCGGGCGG | ACCGACTGGC | GGGTGTCTGG  | GGGCGGGTAA  |
| 561  | GACGTCAATA  | ATGACGTATG  | TTCCCATAGT  | AACGCCAATA | GGGACTTTCC | ATTGACGTCA | ATGGGTGGAG  | TATTTACGGT  |
|      | CTGCAGTTAT  | TACTGCATAC  | AAGGGTATCA  | TTGCGGTTAT | CCCTGAAAGG | TAACTGCAGT | TACCCACCTC  | ATAAATGCCA  |
| 641  | AAATGCCCCA  | CTTGGCAGTA  | CATCAAGTGT  | ATCATATGCC | AAGTCCGCCC | CCTATTGACG | TCAATGACGG  | TAAATGGCCC  |
|      | TTTGACGGGT  | GAACCGTCAT  | GTAGTTTACA  | TAGTATACGG | TTCAGGCGGG | GGATAACTGC | AGTTACTGCC  | ATTTACCGGG  |
| 721  | GCCTGGCATT  | ATGCCCAGTA  | CATGACCTTA  | CGGGACTTTC | CTACTTGGCA | GTACATCTAC | GTATTAGTCA  | TCGCTATTAC  |
|      | CGGACCGTAA  | TACGGGTCAT  | GTAAGTGAAT  | GCCCTGAAAG | GATGAACCGT | CATGTAGATG | CATAATCAGT  | AGCGATAATG  |
| 801  | CATGGTGTATG | CGGTTTTGGC  | AGTACACCAA  | TGGGCGTGGA | TAGCGGTTTG | ACTCACGGGG | ATTTCCAAGT  | CTCCACCCCA  |
|      | GTACCACTAC  | GCCAAAACCG  | TCATGTGGTT  | ACCCGCACCT | ATCGCCAAAC | TGAGTGCCCC | TAAAGGTTCA  | GAGGTGGGGT  |
| 881  | TTGACGTCAA  | TGGGAGTTTG  | TTTTGGCACC  | AAAATCAACG | GGACTTTCCA | AAATGTCGTA | ATAACCCCGC  | CCCGTTGACG  |
|      | AACTGCAGTT  | ACCCCTCAAAC | AAAACCGTGG  | TTTTAGTTGC | CCTGAAAGGT | TTTACAGCAT | TATTGGGGCG  | GGGCAACTGC  |
| 961  | CAAATGGGCG  | GTAGGCGTGT  | ACGGTGGGAG  | GTCTATATAA | CGACAGCTCG | TTTAGTGAAC | CGTCAGATCG  | CCTGGAGACG  |
|      | GTTTACCCGC  | CATCCGCACA  | TGCCACCCTC  | CAGATATATT | CGTCTCGAGC | AAATCACTTG | GCAGTCTAGC  | GGACCTCTGC  |
| 1041 | CCATCCACGC  | TGTTTTGACC  | TCCATAGAAG  | ACACCGGGAC | CGATCCAGCC | TCCGCGGCGG | GGAACGGTGC  | ATTGGAACGC  |
|      | GGTAGGTGCG  | ACAAAACCTG  | AGGTATCTTC  | TGTGGCCCTG | GCTAGGTGCG | AGGCGCCGGC | CCTTGCCACG  | TAACCTTGCG  |
| 1121 | GGATTCCCCG  | TGCCAAGAGT  | GACGTAAGTA  | CCGCCTATAG | ACTCTATAGG | CACACCCCTT | TGGCTCTTAT  | GCATGCTATA  |
|      | CCTAAGGGGC  | ACGGTTCTCA  | CTGCATTTCAT | GGCGGATATC | TGAGATATCC | GTGTGGGGAA | ACCGAGAATA  | CGTACGATAT  |
| 1201 | CTGTTTTTGG  | CTTGGGGCCT  | ATACACCCCC  | GTCCTTTATG | CTATAGGTGA | TGGTATAGCT | TAGCCTATAG  | GTGTGGGTTA  |
|      | GACAAAAACC  | GAACCCCGGA  | TATGTGGGGG  | CGAGGAATAC | GATATCCACT | ACCATATCGA | ATCGGATATC  | CACACCCAAT  |
| 1281 | TTGACCATT   | TTGACCACTC  | CCCTATTGGT  | GACGATACTT | TCCATTACTA | ATCCATAACA | TGGCTCTTTG  | CCACAACAT   |
|      | AACTGGTAAT  | AACTGGTGAG  | GGGATAACCA  | CTGCTATGAA | AGGTAATGAT | TAGGTATTGT | ACCGAGAAAC  | GGTGTGATA   |
| 1361 | CTCTATTGGC  | TATATGCCAA  | TACTCTGTCC  | TTCAGAGACT | GACACGGACT | CTGTATTTT  | ACAGGATGGG  | GTCCATTIAT  |
|      | GAGATAACCG  | ATATACGGTT  | ATGAGACAGG  | AAGTCTCTGA | CTGTGCTGTA | GACATAAAAA | TGTCCTACCC  | CAGGTAATA   |
| 1441 | TATTTACAAA  | TTCACATATA  | CAACAACGCC  | GTCCCCCGTG | CCCGCAGTTT | TTATTAAACA | TAGCGTGGGA  | TCTCCGACAT  |
|      | ATAAATGTTT  | AAGTGTATAT  | GTTGTTGCGG  | CAGGGGGCAC | GGGCGTCAAA | AATAATTTGT | ATCGCACCCCT | AGAGGCTGTA  |



## pCMV - II

## FIGURE 7 - Page 2

|                                                           |            |             |            |            |            |            |            |             |
|-----------------------------------------------------------|------------|-------------|------------|------------|------------|------------|------------|-------------|
| 1521                                                      | CTCGGGTACG | TGTTCCGGAC  | ATGGGCTCTT | CTCCGGTAGC | GGCGGAGCTT | CCACATCCGA | GCCCTGGTCC | CATCCGTCCA  |
|                                                           | GAGCCCATGC | ACAAGGCCCTG | TACCCGAGAA | GAGGCCATCG | CCGCCTCGAA | GGTGTAGGCT | CGGGACCAGG | GTAGGCAGGT  |
| 1601                                                      | GCGGCTCATG | GTGCTCCGGC  | AGCTCCTTGC | TCCTAACAGT | GGAGGCCAGA | CTTAGGCACA | GCACAATGCC | CACCACCACC  |
|                                                           | CGCCGAGTAC | CAGCGAGCCG  | TCGAGGAACG | AGGATTGTCA | CCTCCGGTCT | GAATCCGTGT | CGTGTTACGG | GTGGTGGTGG  |
| 1681                                                      | AGTGTGCCGC | ACAAGGCCGT  | GGCGGTAGGG | TATGTGTCTG | AAAATGAGCT | CGGAGATTGG | GCTCGCACCT | GGACGCAGAT  |
|                                                           | TCACACGGCG | TGTTCCGGCA  | CCGCCATCCC | ATACACAGAC | TTTACTCGA  | GCCTCTAACC | CGAGCGTGGG | CCTGCGTCTA  |
| 1761                                                      | GGAAGACTTA | AGGCAGCGGC  | AGAAGAAGAT | GCAGGCAGCT | GAGTTGTTGT | ATTCTGATAA | GAGTCAGAGG | TAACCTCCCGT |
|                                                           | CCTTCTGAAT | TCCGTCCGCG  | TCTTCTTCTA | CGTCCGTCGA | CTCAACAACA | TAAGACTATT | CTCAGTCTCC | ATTGAGGGCA  |
| 1841                                                      | TGCGGTGCTG | TTAACGGTGG  | AGGGCAGTGT | AGTCTGAGCA | GTAATCGTTG | CTGCCGCGCG | CGCCACCAGA | CATAATAGCT  |
|                                                           | ACGCCACGAC | AATTGCCACC  | TCCCGTCACA | TCAGACTCGT | CATGAGCAAC | GACGGCGCGC | GCGGTGGTCT | GTATTATCGA  |
| EcoRI                                                     |            |             |            |            |            |            |            |             |
| 1921                                                      | GACAGACTAA | CAGACTGTTC  | CTTCCATGG  | GTCCTTCTG  | CAGTCACCGT | CGTCGACCTA | AGAATTCAGA | CTCGAGCAAG  |
|                                                           | CTGTCTGATT | GTCTGACAA   | GAAAGGTACC | CAGAAAAGAC | GTGAGTGGCA | GCAGCTGGAT | TCTTAAGTCT | GAGCTCGTTC  |
| XbaI                      BamHI                      MluI |            |             |            |            |            |            |            |             |
| 2001                                                      | TCTAGAAAAG | CGCGCCAAGA  | TATCAAGCAT | CCACTACGCG | TTAGAGCTCG | CTGATCAGCC | TCGACTGTGC | CTTCTAGTTG  |
|                                                           | AGATCTTTCC | GCGCGTTTCT  | ATAGTTTCTA | GGTGTGCGC  | AATCTCGAGC | GACTAGTCGG | AGCTGACACG | GAAGATCAAC  |
| 2081                                                      | CCAGCCATCT | GTTGTTTGGC  | CCTCCCCCGT | GCCTTCCTTG | ACCCTGGAAG | GTGCCACTCC | CACTGTCTTT | TCCTAATAAA  |
|                                                           | GGTCGGTAGA | CAACAAACGG  | GGAGGGGGCA | CGGAAGGAAC | TGGGACCTTC | CACGGTGAGG | GTGACAGGAA | AGGATTATTT  |
| 2161                                                      | ATGAGGAAAT | TGCATCGCAT  | TGTCTGAGTA | GGTGTCAATC | TATTCTGGGG | GGTGGGGTGG | GGCAGGACAG | CAAGGGGGAG  |
|                                                           | TACTCCTTTA | ACGTAGCGTA  | ACAGACTCAT | CCACAGTAAG | ATAAGACCCC | CCACCCACCC | CCGTCCTGTC | GTTCCCCCTC  |
| 2241                                                      | GATTGGGAAG | ACAATAGCAG  | GCATGCTGGG | GAGCTCTTCC | GCTTCCTCGC | TCAGTGACTC | GCTGCGCTCG | GTGTTCCGGC  |
|                                                           | CTAACCCCTT | TGTTATCGTC  | CGTACGACCC | CTCGAGAAGG | CGAAGGAGCG | AGTGACTGAG | CGACGCGAGC | CAGCAAGCCG  |
| 2321                                                      | TGCGGCGAGC | GGTATCAGCT  | CACTCAAAGG | CGGTAATACG | GTTATCCACA | GAATCAGGGG | ATAACGCAGG | AAAGAACATG  |
|                                                           | ACGCGCGCTG | CCATAGTCGA  | GTGAGTTTCC | GCCATTATGC | CAATAGGTGT | CTTAGTCCCC | TATTGCGTCC | TTTCTTGATC  |
| 2401                                                      | TGAGCAAAAG | GCCAGCAAAA  | GGCCAGGAAC | CGTAAAAAGG | CCGCGTTGCT | GGCGTTTTTC | CATAGGCTCC | GCCCCCTGTA  |
|                                                           | ACTCGTTTTT | CGGTCGTTTT  | CCGGTCCTTG | GCATTTTTTC | GGCGCAACGA | CCGCAAAAAG | GTATCCGAGG | CGGGGGGACT  |
| 2481                                                      | CGAGCATCAC | AAAAATCGAC  | GCTCAAGTCA | GAGGTGGCGA | AACCCGACAG | GACTATAAAG | ATACCAGGCG | TTTCCCCCTG  |
|                                                           | GCTCGTAGTG | TTTTTAGCTG  | CGAGTTCAGT | CTCCACCGCT | TTGGGCTGTC | CTGATATTTC | TATGGTCCGC | AAAGGGGGAC  |
| 2561                                                      | GAAGCTCCCT | CGTGCGCTCT  | CCTGTTCCGA | CCCTGCCGCT | TACCGGATAC | CTGTCCGCCT | TTCTCCCTTC | GGGAAGCGTG  |
|                                                           | CTTCGAGGGA | GCACGCGAGA  | GGACAAGGCT | GGGACGGCGA | ATGGCCTATG | GACAGGCGGA | AAGAGGGAAG | CCCTTCGCAC  |
| 2641                                                      | GCGCTTTCTC | AATGCTCAGC  | CTGTAGGTAT | CTCAGTTCGG | TGTAGGTCGT | TCGCTCCAAG | CTGGGCTGTG | TGCACGAACC  |
|                                                           | CGCGAAAGAG | TTACGAGTGC  | GACATCCATA | GAGTCAAGCC | ACATCCAGCA | AGCGAGGTTC | GACCCGACAC | ACGTGCTTGG  |
| 2721                                                      | CCCCGTTTCA | CCCGACCGCT  | GCGCCTTATC | CGGTAACAT  | CGTCTTGAGT | CCAACCCGGT | AAGACACGAC | TTATCGCCAC  |
|                                                           | GGGGCAAGTC | GGGCTGGCGA  | CGCGGAATAG | GCCATTGATA | GCAGAACTCA | GGTTGGGCCA | TTCTGTGCTG | AATAGCGGTG  |
| 2801                                                      | TGGCAGCAGC | CACTGGTAAC  | AGGATTAGCA | GAGCGAGGTA | TGTAGGCGGT | GCTACAGAGT | TCTTGAAGTG | GTGGCCTAAC  |
|                                                           | ACCGTCGTGC | GTGACCATTG  | TCCTAATCGT | CTCGCTCCAT | ACATCCGCCA | CGATGTCTCA | AGAACTTCAC | CACCGGATTG  |
| 2881                                                      | TACGGCTACA | CTAGAAGGAC  | AGTATTTGGT | ATCTGCGCTC | TGCTGAAGCC | AGTTACCTTC | GGAAAAAGAG | TTGGTAGCTC  |
|                                                           | ATGCCGATGT | GATCTTCTCG  | TCATAAACCA | TAGACGGCAG | ACGACTTCGG | TCAATGGAAG | CCTTTTCTC  | AACCATCGAG  |

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## FIGURE 7 - Page 3

2961 TTGATCCGGC AAACAAACCA CCGCTGGTAG CGGTGGTTTT TTTGTTTGCA AGCAGCAGAT TACGCGCAGA AAAAAAGGAT  
AACTAGGCCG TTTGTTTGGT GCGGACCATC GCCACCAAAA AAACAAACGT TCGTCGTCTA ATGCGCGTCT TTTTTCCTA

---

3041 CTCAAGAAGA TCCTTTGATC TTTTCTACGG GGTCTGACGC TCAGTGGAAAC GAAAACTCAC GTTAAGGGAT TTTGGTCATG  
GAGTTCTTCT AGGAAACTAG AAAAGATGCC CCAGACTGCG AGTCACCTTG CTTTGTAGTG CAATTCCTTA AAACCAAGTAC

---

3121 AGATTATCAA AAAGGATCTT CACCTAGATC CTTTAAATTT AAAAATGAAG TTTTAAATCA ATCTAAAGTA TATATGAGTA  
TCTAATAGTT TTTCTAGAA GTGGATCTAG GAAAATTTAA TTTTACTTTC AAAATTTAGT TAGATTTTAT ATATACTCAT

---

3201 AACTTGGTCT GACAGTTACC AATGCTTAAT CAGTGAGGCA CCTATCTCAG CGATCTGTCT ATTTCTGTTCA TCCATAGTTG  
TTGAACCAGA CTGTCAATGG TTACGAATTA GTCACCTCCG GGATAGAGTC GCTAGACAGA TAAAGCAAGT AGGTATCAAC

---

3281 CCTGACTCCC CGTCGTGTAG ATAACACGA TACGGGAGGG CTTACCATCT GGCCCCAGTG CTGCAATGAT ACCGCGAGAC  
GGACTGAGGG GCAGCACATC TATTGATGCT ATGCCCTCCC GAATGGTAGA CCGGGGTCAC GACGTTACTA TGGCGCTCTG

---

3361 CCACGCTCAC CGGCTCCAGA TTTATCAGCA ATAAACCAGC CAGCCGGAAG GGCCGAGCGC AGAAGTGGTC CTGCAACTTT  
GGTGCAGATG GCCGAGGTCT AAATAGTCGT TATTTGGTCG GTCGGCCTTC CCGGCTCGCG TCTTCACCAG GACGTTGAAA

---

3441 ATCCGCCTCC ATCCAGTCTA TTAATTGTTG CCGGGAAGCT AGAGTAAGTA GTTCGCCAGT TAATAGTTTG CGCAACGTTG  
TAGGCGGAGG TAGGTCAGAT AATTAACAAC GGCCCTTCGA TCTATTCTAT CAAGCGGTCA ATTATCAAAC GCGTTGCAAC

---

3521 TTGCCATTGC TACAGGCATC GTGGTGTAC GTCGTCGTT TGGTATGGCT TCATTACGCT CCGGTTCCCA ACGATCAAGG  
AACGGTAACG ATGTCGGTAG CACCACAGTG CGAGCAGCAA ACCATACCGA AGTAAGTCGA GGCCAAGGGT TGCTAGTTCC

---

3601 CGAGTTACAT GATCCCCAT GTTGTGCAAA AAAGCGGTTA GCTCCTTCGG TCCTCCGATC GTTGTGAGAA GTAAGTTGGC  
GCTCAATGTA CTAGGGGGTA CAACACGTTT TTTCCGCAAT CGAGGAAGCC AGGAGGCTAG CAACAGTCTT CATTCAACCG

---

3681 CGCAGTGTTA TCACTCATGG TTATGGCAGC ACTGCATAAT TCTCTTACTG TCATGCCATC CGTAAGATGC TTTTCTGTGA  
GCGTCACAAT AGTGAGTACC AATACCGTCG TGACGTATTA AGAGAATGAC AGTACGGTAG GCATTCTACG AAAAGACACT

---

3761 CTGGTGAGTA CTCAACCAAG TCATTCTGAG AATAGTGTAT GCGGCGACCG AGTTGCTCTT GCCCGGCGTC AATACGGGAT  
GACCACTCAT GAGTTGGTTC AGTAAGACTC TTATCACATA CGCCGCTGGC TCAACGAGAA CCGGCGCGAG TTATGCCCTA

---

3841 AATACCGCGC CACATAGCAG AACTTTAAAA GTGCTCATCA TTGGAACACG TTCTTCGGGG CGAAACTCTT CAAGGATCTT  
TTATGGCGCG GTGTATCGTC TTGAAATTTT CACGAGTAGT AACCTTTTGC AAGAAGCCCC GCTTTTGTGA GTTCCTAGAA

---

3921 ACCGCTGTTG AGATCCAGTT CGATGTAACG CACTCGTGCA CCAACTGAT CTTCAGCATC TTTTACTTTC ACCAGCGTTT  
TGCGGACAAC TCTAGGTCAA GCTACATTGG GTGAGCACGT GGGTTGACTA GAAGTCGTAG AAAATGAAAG TGCTCGCAAA

---

4001 CTGGGTGAGC AAAAACAGGA AGGCAAAATG CCGCAAAAAA GGAATAAGG GCGACACGGA AATGTTGAAT ACTCATACTC  
GACCACTCG TTTTGTCTCT TCCGTTTAC GCGGTTTTTT CCCTTATTCC CGCTGTGCCT TTACAACCTA TGAGTATGAG

---

4081 TTCCTTTTTC AATATTATTG AAGCATTAT CAGGGTTATT GTCTCATGAG CGGATACATA TTTGAATGTA TTTAGAAAAA  
AAGGAAAAAG TTATAATAAC TTCGTAAATA GTCCCAATAA CAGAGTACTC GCCTATGTAT AAACCTTACAT AAATCTTTT

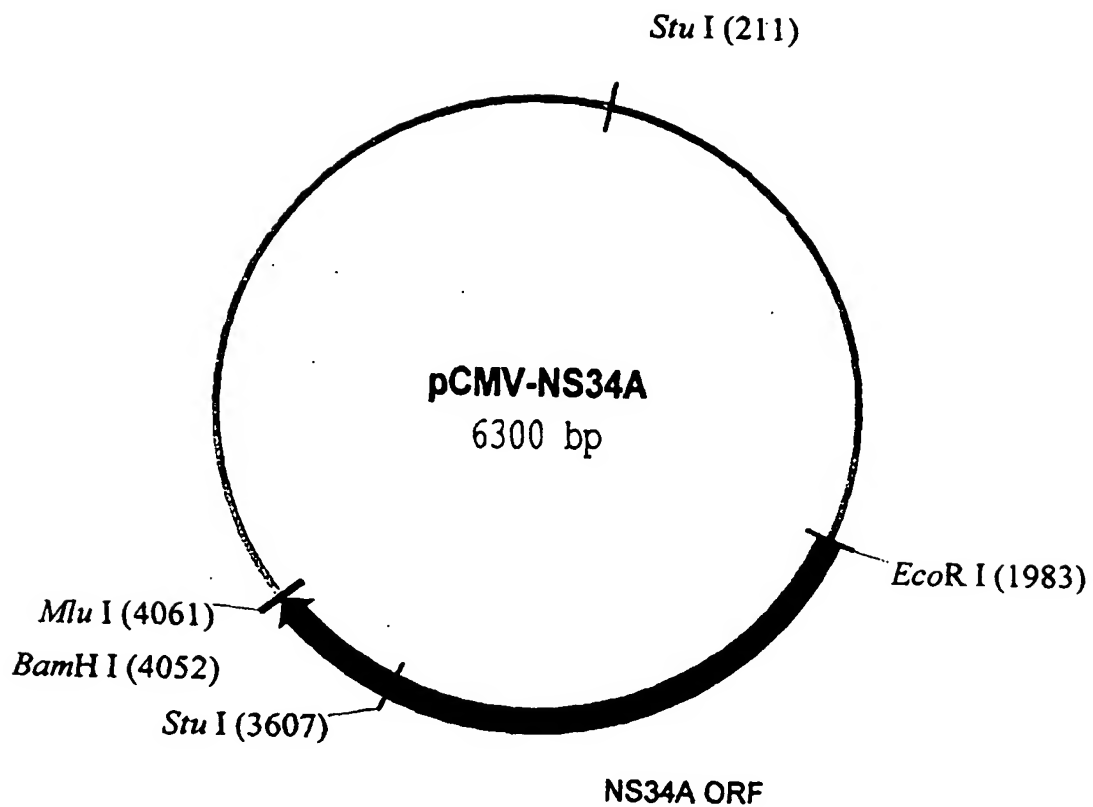
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4161 TAAACAAATA GGGGTTCGCG GCACATTTC CCGAAAAGTG CCACCTGACG TCTAAGAAAC CATTATTATC ATGACATTAA  
ATTTGTTTAT CCCCAGGCG CGTGTAAGG GCGTTTTCAC GGTGGACTGC AGATTCTTTG GTAATAATAG TACTGTAATT

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4241 CCTATAAAAA TAGGCGTATC ACGAGGCCCT TTCGTC  
GGATATTTTT ATCCGCATAG TGCTCCGGGA AAGCAG

**FIGURE 8**



pCMV-NS34A

## FIGURE 9 - Page 1

|       |            |            |            |            |             |
|-------|------------|------------|------------|------------|-------------|
|       | TCGCGCGTTT | CGGTGATGAC | GGTGAAAACC | TCTGACACAT | GCAGCTCCCG  |
|       | AGCGCGCAAA | GCCACTACTG | CCACTTTTGG | AGACTGTGTA | CGTCGAGGGC  |
| <hr/> |            |            |            |            |             |
| 51    | GAGACGGTCA | CAGCTTGTCT | GTAAGCGGAT | GCCGGGAGCA | GACAAGCCCG  |
|       | CTCTGCCAGT | GTCGAACAGA | CATTCGCCTA | CGGCCCTCGT | CTGTTCCGGC  |
| <hr/> |            |            |            |            |             |
| 101   | TCAGGCGCGG | TCAGCGGGTG | TTGGCGGGTG | TCGGGGCTGG | CTTAACATATG |
|       | AGTCCCGCGC | AGTCGCCCAC | AACCGCCCAC | AGCCCCGACC | GAATTGATAC  |
| <hr/> |            |            |            |            |             |
| 151   | CGGCATCAGA | GCAGATTGTA | CTGAGAGTGC | ACCATATGAA | GCTTTTTGCA  |
|       | GCCGTAGTCT | CGTCTAACAT | GACTCTCAGC | TGGTATACTT | CGAAAAACGT  |
| <hr/> |            |            |            |            |             |
|       | StuI       |            |            |            |             |
|       | -----      |            |            |            |             |
| 201   | AAAGCCTAGG | CCTCCAAAAA | AGCCTCCTCA | CTACTTCTGG | AATAGCTCAG  |
|       | TTTCGGATCC | GGAGGTTTTT | TCGGAGGAGT | GATGAAGACC | TTATCGAGTC  |
| <hr/> |            |            |            |            |             |
| 251   | AGGCCGAGGC | GGCCTCGGCC | TCTGCATAAA | TAAAAAAAT  | TAGTCAGCCA  |
|       | TCCGGCTCCG | CCGGAGCCCG | AGACGTATTT | ATTTTTTTTA | ATCAGTCGGT  |
| <hr/> |            |            |            |            |             |
| 301   | TGGGGCGGAG | AATGGGCGGA | ACTGGGCGGG | GAGGGAATTA | TTGGCTATTG  |
|       | ACCCCGCCTC | TTACCCGCCT | TGACCCGCCC | CTCCCTTAAT | AACCGATAAC  |
| <hr/> |            |            |            |            |             |
| 351   | GCCATTGCAT | ACGTTGTATC | TATATCATAA | TATGTACATT | TATATTGGCT  |
|       | CGGTAACGTA | TGCAACATAG | ATATAGTATT | ATACATGTAA | ATATAACCGA  |
| <hr/> |            |            |            |            |             |
| 401   | CATGTCCAAT | ATGACCGCCA | TGTTGACATT | GATTATTGAC | TAGTTATTAA  |
|       | GTACAGGTTA | TACTGGCGGT | ACAACTGTAA | CTAATAACTG | ATCAATAATT  |
| <hr/> |            |            |            |            |             |
| 451   | TAGTAATCAA | TTACGGGGTC | ATTAGTTCAT | AGCCCATATA | TGGAGTICCG  |
|       | ATCATTAGTT | AATGCCCCAG | TAATCAAGTA | TCGGGTATAT | ACCTCAAGGC  |
| <hr/> |            |            |            |            |             |
| 501   | CGTACATAA  | CTTACGGTAA | ATGGCCCGCC | TGGCTGACCG | CCCAACGACC  |
|       | GCAATGTATT | GAATGCCATT | TACCGGGCGG | ACCGACTGGC | GGGTTGCTGG  |
| <hr/> |            |            |            |            |             |
| 551   | CCCGCCCAT  | GACGTCAATA | ATGACGTATG | TCCCATAGT  | AACGCCAATA  |
|       | GGCGGGGTAA | CTGCAGTTAT | TACTGCATAC | AAGGGTATCA | TTGCGGTTAT  |
| <hr/> |            |            |            |            |             |
| 601   | GGGACTTTC  | ATTGACGTCA | ATGGGTGGAG | TATTTACGGT | AACTGCCCCA  |
|       | CCCTGAAAGG | TAACTGCAGT | TACCCACCTC | ATAAATGCCA | TTTGACGGGT  |
| <hr/> |            |            |            |            |             |
| 651   | CTTGGCAGTA | CATCAAGTGT | ATCATATGCC | AAGTCCGCCC | CCTATTGACG  |
|       | GAACCGTCAT | GTAGTTCACA | TAGTATACGG | TTGAGGCGGG | GGATAACTGC  |
| <hr/> |            |            |            |            |             |
| 701   | TCAATGACGG | TAAATGGCCC | GCCTGGCATT | ATGCCCAGTA | CATGACCTTA  |
|       | AGTTACTGCC | ATTTACCGGG | CGGACCGTAA | TACGGGTCAT | GTACTGGAAT  |
| <hr/> |            |            |            |            |             |
| 751   | CGGGACTTTC | CTACTTGCCA | GTACATCTAC | GTATTAGTCA | TCGCTATTAC  |
|       | GCCCTGAAAG | GATGAACCGT | CATGTAGATG | CATAATCAGT | AGCGATATG   |
| <hr/> |            |            |            |            |             |
| 801   | CATGGTGATG | CGGTTTTGGC | AGTACACCAA | TGGGCGTGGA | TAGCGGTTTG  |
|       | GTACCACTAC | GCCAAAACCG | TCATGTGGTT | ACCCGCACCT | ATCGCCAAAC  |
| <hr/> |            |            |            |            |             |
| 851   | ACTCACGGGG | ATTTCCAAGT | CTCCACCCCA | TTGACGTCAA | TGGGAGTTTG  |
|       | TGAGTGCCCC | TAAAGGTTCA | GAGGTGGGGT | AACTGCAGTT | ACCCTCAAAC  |

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## FIGURE 9 - Page 2

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901  TTTTGGCACC AAAATCAACG GGACTTTCCA AAATGTCGTA ATAACCCCGC
    AAAACCGTGG TTTTAGTTGC CCTGAAAGGT TTTACAGCAT TATTGGGGCG

951  CCCGTTGACG CAAATGGGCG GTAGGCGTGT ACGGTGGGAG GTCTATATAA
    GGGCAACTGC GTTTACCCGC CATCCGCACA TGCCACCCTC CAGATATATT

1001 GCAGAGCTCG TTTAGTGAAC CGTCAGATCG CCTGGAGACG CCATCCACGC
    CGTCTCGAGC AAATCACTTG GCAGTCTAGC GGACCTCTGC GGTAGGTGCG

1051 TGTTTTGACC TCCATAGAAG ACACCGGGAC CGATCCAGCC TCCGCGGCCG
    ACAAACTGG AGGTATCTTC TGTGGCCCTG GCTAGGTCGG AGGCGCCGGC

1101 GGAACGGTGC ATTGGAACGC GGATTCCCCG TGCCAAGAGT GACGTAAGTA
    CCTTGCCACG TAACCTTGCG CCTAAGGGGC ACGGTTCTCA CTGCATTAT

1151 CCGCCTATAG ACTCTATAGG CACACCCCTT TGGCTCTTAT GCATGCTATA
    GCGGATATC TGAGATATCC GTGTGGGGAA ACCGAGAATA CGTACGATAT

1201 CTGTTTTTGG CTTGGGGCCT ATACACCCCC GCTCCTTATG CTATAGGTGA
    GACAAAAACC GAACCCCGGA TATGTGGGGG CGAGGAATAC GATATCCACT

1251 TGGTATAGCT TAGCCTATAG GTGTGGGTTA TTGACCATTA TTGACCACTC
    ACCATATCGA ATCGGATATC CACACCCAAT AACTGGTAAT AACTGGTGAG

1301 CCCTATTGGT GACGATACTT TCCATTACTA ATCCATAACA TGGCTCTTTG
    GGGATAACCA CTGCTATGAA AGGTAATGAT TAGGTATTGT ACCGAGAAAC

1351 CCACAACATAT CTCTATTGGC TATATGCCAA TACTCTGTCC TTCAGAGACT
    GGTGTTGATA GAGATAACCG ATATACGGTT ATGAGACAGG AAGTCTCTGA

1401 GACACGGACT CTGTATTTTT ACAGGATGGG GTCCATTTAT TATTTACAAA
    CTGTGCCTGA GACATAAAAA TGTCTTACCC CAGGTAATA ATAAATGTTT

1451 TTCACATATA CAACAACGCC GTCCCCCGTG CCGCGAGTTT TTATTAACA
    AAGTGATATAT GTTGTGCGG CAGGGGGCAC GGGCGTCAA AATAATTTGT

1501 TAGCGTGGGA TCTCCGACAT CTCGGGTACG TGTCCGGAC ATGGGCTCTT
    ATCGCACCTT AGAGGCTGTA GAGCCCATGC ACAAGGCCTG TACCCGAGAA

1551 CTCGGGTAGC GCGGAGCTT CCACATCCGA GCCCTGGTCC CATCCGTCCA
    GAGGCCATCG CCGCTCGAA GGTGTAGGCT CGGGACCAGG GTAGGCAGGT

1601 GCGGCTCATG GTCGCTCGGC AGCTCCTTGC TCCTAACAGT GGAGGCCAGA
    CGCCGAGTAC CAGCGAGCCG TCGAGGAACG AGGATTGTCA CCTCCGGTCT

1651 CTTAGGCACA GCACAATGCC CACCACCACC AGTGTGCCGC ACAAGGCCGT
    GAATCCGTGT CGTGTTACGG GTGGTGGTGG TCACACGGCG TGTTCGGCA

1701 GCGGGTAGGG TATGTGTCTG AAAATGAGCT CGGAGATTGG GCTCGCACCT
    CCGCCATCCC ATACACAGAC TTTTACTCGA GCCTCTAACC CGAGCGTGGA

1751 GGACGCAGAT GGAAGACTTA AGGCAGCGGC AGAAGAAGAT GCAGGCAGCT
    CCTGCGTCTA CTTTCTGAAT TCCGTGCGCG TCTTCTTCTA CGTCCGTCTGA

1801 GAGTTGTTGT ATTCTGATAA GAGTCAGAGG TAACTCCCGT TCGGGTGCTG
    CTAACAACA TAAGACTATT CTCAGTCTCC ATTGAGGGCA ACGCCACGAC

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## FIGURE 9 - Page 3

1851 TTAACGGTGG AGGGCAGTGT AGTCTGAGCA GTACTCGTTG CTGCCGCGCG  
AATTGCCACC TCCCGTCACA TCAGACTCGT CATGAGCAAC GACGGCGCGC

1901 CGCCACCAGA CATAATAGCT GACAGACTAA CAGACTGTTC CTTTCCATGG  
GCGGTGGTCT GTATTATCGA CTGTCTGATT GTCTGACAAG GAAAGGTACC

+2

M A P

EcoRI

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1951 GTCTTTTCTG CAGTCACCGT CGTCGACCTA AGAATTCACC ATGGCGCCCA  
CAGAAAAGAC GTCAGTGGCA GCAGCTGGAT TCTTAAGTGG TACCGCGGGT

+2

2001 I T A Y A Q Q T R G L L G C I I T  
TCACGGCGTA CGCCGAGCAG ACAAGGGGCC TCCTAGGGTG CATAATCACC  
AGTGCCGCAT GCGGGTCGTC TGTTCGCCGG AGGATCCAC GTATTAGTGG

+2

2051 S L T G R D K N Q V E G E V Q I V  
AGCCTAACTG GCCGGGACAA AAACCAAGTG GAGGGTGAGG TCCAGATTGT  
TCGGATTGAC CGGCCCTGTT TTTGGTTCAC CTCCCACTCC AGGTCTAACA

+2

2101 S T A A Q T F L A T C I N G V C  
GTCAACTGCT GCCCAAACCT TCCTGGCAAC GTGCATCAAT GGGGTGTGCT  
CAGTTGACGA CGGGTTTGA AGGACCGTTG CACGTAGTTA CCCCACACGA

+2

2151 W T V Y H G A G T R T I A S P K G  
GGACTGTCTA CCACGGGGCC GGAACGAGGA CCATCGCGTC ACCCAAGGGT  
CCTGACAGAT GGTGCCCCGG CCTTGCTCCT GGTAGCGCAG TGGTTCCTCA

+2

2201 P V I Q M Y T N V D Q D L V G W P  
CCTGTATCC AGATGTATAC CAATGTAGAC CAAGACCTTG TGGGCTGGCC  
GGACAGTAGG TCTACATATG GTTACATCTG GTTCTGGAAC ACCCGACCGG

+2

2251 A S Q G T R S L T P C T C G S S  
CGCTTCGCAA GGTACCCGCT CATTGACACC CTGCACCTGC GGCTCCTCGG  
GCGAAGCGTT CCATGGGCGA GTAAGTGTGG GACGTGAACG CCGAGGAGCC

+2

2301 D L Y L V T R H A D V I P V R R K  
ACCTTTACCT GGTACAGAGG CACGCCGATG TCATTCCCGT GCGCCGGCGG  
TGGAATGGA CCAGTGCTCC GTGCGGCTAC AGTAAGGGCA CGCGGCCGCC

+2

2351 G D S R G S L L S P R P I S Y L K  
GGTGATAGCA GGGGCAGCCT GCTGTGCCCC CGGCCCATTT CCTACTTGAA  
CCACTATCGT CCCCCTCGGA CGACAGCGGG GCCGGGTAAA GGATGAAC'T

+2

2401 G S S G G P L L C P A G H A V G  
AGGCTCCTCG GGGGGTCCGC TGTTGTGCCC CGCGGGGCAC GCCGTGGGCA  
TCCGAGGAGC CCCCAGGCG ACAACACGGG GCGCCCCGTG CGGCACCCGT

+2

2451 I F R A A V C T R G V A K A V D F  
TATTTAGGGC CGCGGTGTGC ACCCGTGGAG TGGCTAAGGC GGTGGACTTT  
ATAATCCCG GCGCCACACG TGGGCACCTC ACCGATTCCG CCACCTGAAA

+2

2501 I P V E N L E T T M R S P V F T D  
ATCCCTGTGG AGAACCTAGA GACAACCATG AGGTCCCCGG TGTTACGGA  
TAGGGACACC TCTTGATCT CTGTTGGTAC TCCAGGGGCC ACAAGTGCCT

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## FIGURE 9 - Page 4

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+2 N S S P P V V P Q S F Q V A H L
2551 TAACTCCTCT CCACCAGTAG TGCCCCAGAG CTTCCAGGTG GCTCACCTCC
ATTGAGGAGA GGTGGTCATC ACGGGGTCTC GAAGGTCCAC CGAGTGGAGG

+2 H A P T G S G K S T K V P A A Y A
2601 ATGCTCCAC AGGCAGCGGC AAAAGCACCA AGGTCCCGGC TGCATATGCA
TACGAGGGTG TCCGTCGCCG TTTTCGTGGT TCCAGGGCCG ACGTATACGT

+2 A Q G Y K V L V L N P S V A A T L
2651 GCTCAGGGGT ATAAGGTGCT AGTACTCAAC CCCTCTGTG CTGCAACACT
CGAGTCCCGA TATTCCACGA TCATGAGTTG GGGAGACAAC GACGTTGTGA

+2 G F G A Y M S K A H G I D P N I
2701 GGGCTTTGGT GCTTACATGT CCAAGGCTCA TGGGATCGAT CCTAACATCA
CCCGAAACCA CGAATGTACA GGTCCGAGT ACCCTAGCTA GGATTGTAGT

+2 R T G V R T I T T G S P I T Y S T
2751 GGACCGGGGT GAGAACAAAT ACCACTGGCA GCCCATCAC GTACTCCACC
CCTGGCCCCA CTCTGTAA TGGTGACCGT CGGGGTAGTG CATGAGGTGG

+2 Y G K F L A D G G C S G G A Y D I
2801 TACGGCAAGT TCCTTGCCGA CGGCGGGTGC TCGGGGGGCG CTTATGACAT
ATGCCGTTCA AGGRACGGCT GCCGCCACG AGCCCCCGC GAATACTGTA

+2 I I C D E C H S T D A T S I L G
2851 AATAATTTGT GACGAGTGCC ACTCCACGGA TGCCACATCC ATCTTGGGCA
TTATTAAACA CTGCTCACGG TGAGGTGCCT ACGGTGTAGG TAGAACCCGT

+2 I G T V L D Q A E T A G A R L V V
2901 TTGGCACTGT CTTGACCAA GCAGAGACTG CGGGGGCGAG ACTGGTTGTG
AACCGTGACA GGAAGTGGT CGTCTCTGAC GCCCCCGCTC TGACCAACAC

+2 L A T A T P P G S V T V P H P N I
2951 CTGCCACCG CCACCCCTCC GGGCTCCGTC ACTGTGCCCC ATCCCAACAT
GAGCGGTGGC GGTGGGAGG CCCGAGGCAG TGACACGGG TAGGTTGTA

+2 E E V A L S T T G E I P F Y G K
3001 CGAGGAGGTT GCTCTGTCCA CCACCGGAGA GATCCCTTTT TACGGCAAGG
GCTCTCCAA CGAGACAGGT GGTGGCCTCT CTAGGGAAAA ATGCCGTTCC

+2 A I P L E V I K G G R H L I F C H
3051 CTATCCCCCT CGAAGTAATC AAGGGGGGGA GACATCTCAT CTTCTGTCAT
GATAGGGGGA GCTTCATTAG TTCCCCCCT CTGTAGAGTA GAAGACAGTA

+2 S K K K C D E L A A K L V A L G I
3101 TCAAAGAAGA AGTGCGACGA ACTCGCCGCA AAGCTGGTCG CATTGGGCAT
AGTTTCTTCT TCACGCTGCT TGAGCGGCGT TCGACACAGC GTAACCCGTA

+2 N A V A Y Y R G L D V S V I P T
3151 CAATGCCGTG GCCTACTACC GCGGTCTTGA CGTGTCCGTC ATCCCGACCA
GTTACGGCAC CGGATGATG CGCAGAACT GCACAGGCAG TAGGGCTGGT

+2 S G D V V V V A T D A L M T G Y T
3201 GCGGCGATGT TGTGTCGTG GCAACCGATG CCCTCATGAC CGGCTATACC
CGCCGCTACA ACAGCAGCAC CGTTGGCTAC GGGAGTACTG GCCGATATGG

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## FIGURE 9 - Page 5

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+2 G D F D S V I D C N T C V T Q T V
3251 GCGCACTTCG ACTCGGTGAT AGACTGCAAT ACGTGTGTCA CCCAGACAGT
    CCGCTGAAGC TGAGCCACTA TCTGACGTTA TGCACACAGT GGGTCTGTCA

+2 D F S L D P T F T I E T I T L P
3301 CGATTTTCAGC CTTGACCCTA CCTTCACCAT TGAGACAATC ACGCTCCCCC
    GCTAAAGTCG GAACTGGGAT GGAAGTGGTA ACTCTGTTAG TGCGAGGGGG

+2 Q D A V S R T Q R R G R T G R G K
3351 AAGATGCTGT CTCCCGCACT CAACGTCGGG GCAGGACTGG CAGGGGGAAG
    TTCTACGACA GAGGGCGTGA GTTGACGCCC CGTCTGACC GTCCCCCTTC

+2 P G I Y R F V A P G E R P S G M F
3401 CCAGGCATCT ACAGATTGTG GGCACCGGGG GAGCGCCCCT CCGGCATGTT
    GGTCCGTAGA TGTCTAAACA CCGTGGCCCC CTCGCGGGGA GGCCGTACAA

+2 D S S V L C E C Y D A G C A W Y
3451 CCACTCGTCC GTCCTCTGTG AGTGCTATGA CGCAGGCTGT GCTTGGTATG
    GCTGAGCAGG CAGGAGACAC TCACGATACT GCGTCCGACA CGAACCATAC

+2 E L T P A E T T V R L R A Y M N T
3501 AGCTACGCCG CGCCGAGACT ACAGTTAGGC TACGAGCGTA CATGAACACC
    TCGAGTGC GGCGCTCTGA TGTCAATCCG ATGCTCGCAT GTACTTGTGG

+2 P G L P V C Q D H L E F W E G V F
3551 CCGGGGGCTTC CCGTGTGCCA GGACCATCTT GAATTTTGGG AGGGCGTCTT
    GGCCCCGAAG GGCACACGGT CCGTGGTAGAA CTTAAACCC TCCCGCAGAA

+2 T G L T H I D A H F L S Q T K Q
    StuI
    -----
3601 TACAGGCCTC ACTCATATAG ATGCCCACTT TCTATCCCAG ACAAAGCAGA
    ATGTCCGGAG TGAGTATATC TACGGGTGAA AGATAGGGTC TGTTCGTCT

+2 S G E N L P Y L V A Y Q A T V C A
3651 GTGGGGAGAA CCTTCCTTAC CTGGTAGCGT ACCAAGCCAC CGTGTGCGCT
    CACCCCTCTT GGAAGGAATG GACCATCGCA TGGTTCGGTG GCACACCGCA

+2 R A Q A P P P S W D Q M W K C L I
3701 AGGGCTCAAG CCCCTCCCCC ATCGTGGGAC CAGATGTGGA AGTGTITGAT
    TCCCGAGTTC GGGGAGGGGG TAGCACCTCG GTCTACACCT TCACAAACTA

+2 R L K P T L H G P T P L L Y R L
3751 TCGCCTCAAG CCCACCTCC ATGGGCCAAC ACCCTGCTA TACAGACTGG
    AGCGGAGTTC GGGTGGGAGG TACCGGTTG TGGGGACGAT ATGTCTGACC

+2 G A V Q N E I T L T H P V T K Y I
3801 GCGCTGTTC GAATGAAATC ACCCTGACGC ACCCAGTCAC CAAATACATC
    CCGGACAAGT CTTACTTTAG TGGGACTGCG TGGGTCAGTG GTTTATGTAG

+2 M T C M S A D L E V V T S T W V L
3851 ATGACATGCA TGTCGGCCGA CCGGAGGTC GTCACGAGCA CCGGGTGCT
    TACTGTACGT ACAGCCGGCT GGACCTCCAG CAGTGCTCGT GGACCCACGA

+2 V G G V L A A L A A Y C L S T G
3901 CGTTGGCGGC GTCCTGGCTG CTTTGGCCGC GTATTGCCTG TCAACAGGCT
    GCAACCGCCG CAGGACCGAC GAAACCGCG CATAACGGAC AGTTGTCCGA

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**FIGURE 9 - Page 6**

+2 C V V I V G R V V L S G K P A I I  
 3951 GCGTGGTCAT AGTGGGCAGG GTCGTCTTGT CCGGGAAGCC GGCAATCATA  
 CGCACCACTA TCACCCGTCC CAGCAGAACA GGCCCTTCGG CCGTTAGTAT

+2 P D R E V L Y R E F D E M E E C  
 4001 CCTGACAGGG AAGTCCTCTA CCGAGAGTTC GATGAGATGG AAGAGTGCTA  
 GGACTGTCCC TTCAGGAGAT GGCTCTCAAG CTACTCTACC TTCTCAGCAT

BamHI MluI  
 ~~~~~

4051 GGATCCACTA CGCGTTAGAG CTCGCTGATC AGCCTCGACT GTGCCTTCTA
 CCTAGGTGAT GCGCAATCTC GAGCGACTAG TCGGAGCTGA CACGGAAGAT

4101 GTTGCCAGCC ATCTGTTGTT TGCCCTCCC CCGTGCCTTC CTTGACCCTG
 CAACGGTCGG TAGACAACAA ACGGGGAGGG GGCACGGAAG GAACTGGGAC

4151 GAAGGTGCCA CTCCCCTGT CTTTCCTAA TAAATGAGG AAATTGCATC
 CTTCCACGGT GAGGGTGACA GGAAAGGATT ATTTTACTCC TTTAACGTAG

4201 GCATTGTCTG AGTAGGTGTC ATTCTATTCT GGGGGGTGGG GTGGGGCAGG
 CGTAACAGAC TCATCCACAG TAAGATAAGA CCCCCACCC CACCCCGTCC

4251 ACAGCAAGGG GGAGGATTGG GAAGACAATA GCAGGCATGC TGGGGAGCTC
 TGTGCTTCCC CCTCCTAACC CTCTCTTAT CGTCCGTACG ACCCCTCGAG

4301 TTCCGCTTCC TCGCTCACTG ACTCGCTGCG CTCGGTCGTT CGGCTGCGGC
 AAGGCGAAGG AGCGAGTGAC TGAGCGACGC GAGCCAGCAA GCCGACGCCG

4351 GAGCGGTATC AGCTCACTCA AAGGCGGTAA TACGGTTATC CACAGAAATCA
 CTCGCCATAG TCGAGTGAGT TTCCGCCATT ATGCCAATAG GTGTCTTAGT

4401 GGGGATAACG CAGGAAAGAA CATGTGAGCA AAAGGCCAGC AAAAGGCCAG
 CCCCTATTGC GTCCTTTCTT GTACACTCGT TTTCCGGTCG TTTTCCGGTC

4451 GAACCGTAAA AAGGCCGCGT TGCTGGCGTT TTTCCATAGG CTCCGCCCCC
 CTTGGCATT TCCGGCGCA ACGACCGCAA AAAGGTATCC GAGGCGGGGG

4501 CTGACGAGCA TCACAAAAAT CGACGCTCAA GTCAGAGGTG GCGAAACCCG
 GACTGCTCGT AGTGTTTTTA GCTGCGAGTT CAGTCTCCAC CGCTTTGGGC

4551 ACAGGACTAT AAAGATACCA GGCCTTTCCC CCTGGAAGCT CCCTCGTGCG
 TGTCTGATA TTTCTATGGT CCGCAAAGGG GGACCTTCGA GGGAGCACGC

4601 CTCTCCTGTT CCGACCCTGC CGCTTACCGG ATACCTGTCC GCCTTTCTCC
 GAGAGGACAA GGCTGGGACG GCGAATGGCC TATGGACAGG CGGAAAGAGG

4651 CTTCCGGAAG CGTGGCGCTT TCTCAATGCT CACGCTGTAG GTATCTCAGT
 GAAGCCCTTC GCACCGCGAA AGAGTTACGA GTGCGACATC CATAGAGTCA

4701 TCGGTGTAGG TCGTTCGCTC CAAGCTGGGC TGTGTGCACG AACCCCCCGT
 AGCCACATCC AGCAAGCGAG GTTCGACCCG ACACACGTGC TTGGGGGGCA

4751 TCAGCCCGAC CGTGCGCCT TATCCGTAA CTATCGTCTT GAGTCCAACC
 AGTGGGCTG GCGACGCGGA ATAGGCCATT GATAGCAGAA CTCAGGTTGG

4801 CGGTAAGACA CGACTTATCG CCACTGGCAG CAGCCACTGG TAACAGGATT
 GCCATTCTGT GCTGAATAGC GGTGACCGTC GTCGGTGACC ATTGTCTAA

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FIGURE 9 - Page 7

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4851 AGCAGAGCGA GGTATGTAGG CGGTGCTACA GAGTTCTTGA AGTGGTGGCC
    TCGTCTCGCT CCATACATCC GCCACGATGT CTCAAGAACT TCACCACCGG

4901 TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGCTGA
    ATTGATGCCG ATGTGATCTT CCTGTCATAA ACCATAGACG CGAGACGACT

4951 AGCCAGTTAC CTTCGGAAAA AGAGTTGGTA GCTCTTGATC CGGCAAACAA
    TCGGTCAATG GAAGCCTTTT TCTCAACCAT CGAGAACTAG GCCGTTTGTT

5001 ACCACCGCTG GTAGCGGTGG TTTTGTGTT TGCAAGCAGC AGATTACGCG
    TGGTGGCGAC CATCGCCACC AAAAAACAA ACGTTCGTCG TCTAATGCGC

5051 CAGAAAAAAA GGATCTCAAG AAGATCCTTT GATCTTTTCT ACGGGGTCTG
    GTCITTTTTT CCTAGAGTTC TTCTAGGAAA CTAGAAAAGA TGCCCCAGAC

5101 ACGCTCAGTG GAACGAAAAC TCACGTTAAG GGATTTTGGT CATGAGATTA
    TGCGAGTCAC CTTGCTTTTG AGTGCAATTC CCTAAAACCA GTACTCTAAT

5151 TCAAAAAGGA TCTTCACCTA GATCCTTTTA AATTAAAAAT GAAGTTTAA
    AGTTTTCTCT AGAAGTGGAT CTAGGAAAT TTAATTTTTA CTTCAAATTT

5201 ATCAATCTAA AGTATATATG AGTAACTTG GTCTGACAGT TACCAATGCT
    TAGTTAGATT TCATATATAC TCATTGAAC CAGACTGTCA ATGGTTACGA

5251 TAATCAGTGA GGCACCTATC TCAGCGATCT GTCTATTTTG TTCATCCATA
    ATTAGTCACT CCGTGGATAG AGTCGCTAGA CAGATAAAGC AAGTAGGTAT

5301 GTTGCCGTAC TCCCCGTCGT GTAGATAACT ACGATACGGG AGGGCTTACC
    CAACGGACTG AGGGGCAGCA CATCTATTGA TGCTATGCCC TCCCGAATGG

5351 ATCTGGCCCC AGTGCTGCAA TGATACCGCG AGACCCACGC TCACCGGCTC
    TAGACCGGGG TCACGACGTT ACTATGGCGC TCTGGGTGCG AGTGGCCGAG

5401 CAGATTTATC AGCAATAAAC CAGCCAGCCG GAAGGGCCGA GCGCAGAAGT
    GTCTAAATAG TCGTTATTTG GTCGGTCGGC CTTCCCGGCT CGCGTCTTCA

5451 GGTCTGCAA CTTTATCCGC CTCCATCCAG TCTATTAATT GTTGCCGGGA
    CCAGGACGTT GAAATAGGCG GAGGTAGGTC AGATAATTAA CAACGGCCCT

5501 AGCTAGAGTA AGTAGTTCGC CAGTTAATAG TTTGCGCAAC GTTGTGCCA
    TCGATCTCAT TCATCAAGCG GTCAATTATC AAACGCGTTG CAACAACGGT

5551 TTGCTACAGG CATCGTGGTG TCACGCTCGT CGTTTGATAT GGCTTCATTC
    AACGATGTCC GTAGCACCAC AGTGCGAGCA GCAAACCATA CCGAAGTAAG

5601 AGCTCCGGTT CCCAACGATC AAGGCGAGTT ACATGATCCC CCATGTTGTG
    TCGAGGCCAA GGGTTGCTAG TTCCGCTCAA TGTACTAGGG GGTACAACAC

5651 CAAAAAAGCG GTTAGCTCCT TCGGTCCTCC GATCGTTGTC AGAAGTAAGT
    GTTTTTTCGC CAATCGAGGA AGCCAGGAGG CTAGCAACAG TCTTCATTCA

5701 TGGCCGCACT GTTATCACTC ATGGTTATGG CAGCACTGCA TAATTCTCTT
    ACCGGCGTCA CAATAGTGAG TACCAATACC GTCGTGACGT ATTAAGAGAA

5751 ACTGTCAATG CATCCGTAAG ATGCTTTTCT GTGACTGGTG AGTACTCAAC
    TGACAGTACG GTAGGCATTC TACGAAAAGA CACTGACCAC TCATGAGTTG

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FIGURE 9 - Page 8

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5801 CAAGTCATTC TGAGAATAGT GTATGCGGCG ACCGAGTTGC TCTTGCCCGG
    GTTCAGTAAG ACTCTTATCA CATA CGCCGC TGGCTCAACG AGAACGGGCC

5851 CGTCAATACG GGATAATACC GCGCCACATA GCAGAACTTT AAAAGTGCTC
    GCAGTTATGC CCTATTATGG CGCGGTGTAT CGTCTTGAAA TTTTCACGAG

5901 ATCATTGGAA AACGTTCTTC GGGGCGAAAA CTCTCAAGGA TCTTACCGCT
    TAGTAACCTT TTGCAAGAAG CCCCCTTTT GAGAGTTTCT AGAATGGCGA

5951 GTTGAGATCC AGTTCGATGT AACCCACTCG TGCACCCAAC TGATCTTCAG
    CAACTCTAGG TCAAGCTACA TTGGGTGAGC ACGTGGGTTG ACTAGAAGTC

6001 CATCTTTTAC TTTACCAGC GTTCTGGGT GAGCAAAAAC AGGAAGGCAA
    GTAGAAAATG AAAGTGGTCG CAAAGACCCA CTCGTTTTTG TCCTTCCGTT

6051 AATGCCGCAA AAAAGGGAAT AAGGGCGACA CGGAAATGTT GAATACTCAT
    TTACGGCGTT TTTCCCTTA TTCCCGCTGT GCCTTTACAA CTTATGAGTA

6101 ACTCTTCCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGTCTCA
    TGAGAAGGAA AAAGTTATAA TAACTTCGTA AATAGTCCCA ATAACAGAGT

6151 TGAGCGGATA CATATTTGAA TGTATTTAGA AAAATAAACA AATAGGGGTT
    ACTCGCCTAT GTATAAACTT ACATAAATCT TTTTATTTGT TTATCCCCAA

6201 CCGCGCACAT TTCCCCGAAA AGTGCCACCT GACGTCTAAG AAACCATTAT
    GGC GCGTGTA AAGGGGCTTT TCACGGTGGA CTGCAGATTC TTTGGTAATA

6251 TATCATGACA TTAACCTATA AAAATAGGCG TATCAGAGG CCCTTTCGTC
    ATAGTACTGT AATTGGATAT TTTTATCCGC ATAGTGCTCC GGGAAAGCAG

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FIGURE 10

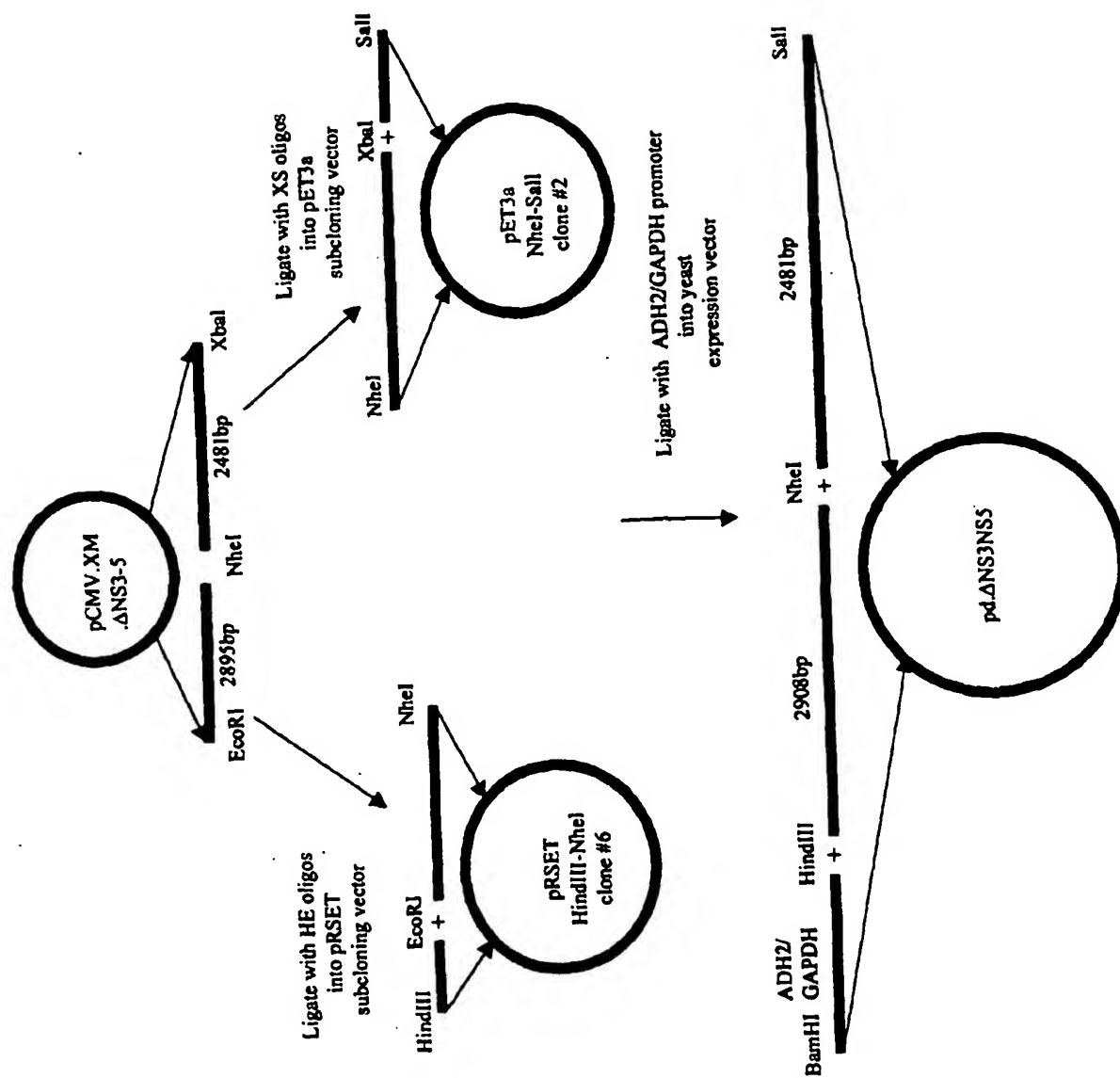


FIGURE 11 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuVal
 2 AGCTTACAAAACAAATTCACCATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTA
 TCGAATGTTTTGTTTAAAGTGGTACCGACGTATACGTTCGAGTCCCGATATTCCACGATCAT
 ^ ^ ^ ^
 1 HIND3, 21 NCOI, 30 NDEI, 58 SCAI,
 LeuAsnProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGly
 62 CTCAACCCCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGG
 GAGTTGGGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCC
 IleAspProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyr
 122 ATCGATCCTAACATCAGGACCGGGGTGAGAACAATTACCACTGGCAGCCCCATCACGTAC
 TAGCTAGGATTGTAGTCCTGGCCCCACTCTTGTTAATGGTGACCGTCGGGGTAGTGCATG
 ^
 122 CLAI,
 SerThrTyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIle
 182 TCCACCTACGGCAAGTTCCTTGCCGACGGCGGTGCTCGGGGGGCGCTTATGACATAATA
 AGGTGGATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGGAATACTGTATTAT
 IleCysAspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeu
 242 ATTTGTGACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGCCTT
 TAAACACTGCTCACGGTGAGGTGCTACGGTGTAGGTAGAACCCGTAACCGTGACAGGAA
 AspGlnAlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGly
 302 GACCAAGCAGAGACTGCGGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGC
 CTGGTTCGTCTCTGACGCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGGAGGCCCCG
 ^
 309 ALWN1,
 SerValThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIle
 362 TCCGTCCTGTGCCCCATCCCAACATCGAGGAGGTGCTCTGTCCACCACCGGAGAGATC
 AGGCAGTGACACGGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAG
 ProPheTyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePhe
 422 CCTTTTACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTC
 GGAAAATGCCGTTCCGATAGGGGAGCTTCATTAGTTCCCCCCTCTGTAGAGTAGAAG
 CysHisSerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsn
 482 TGTCATTCAAAGAAGAAGTGCGACGAACTCGCCGCAAAGCTGGTCGCATTGGGCATCAAT
 ACAGTAAGTTTCTTCTTACGCTGCTTGAGCGCGTTTCGACCAGCGTAACCCGTAGTTA
 AlaValAlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValVal
 542 GCCGTGGCCTACTACCGCGGTCTTGACGTGTCCGTCATCCCGACCAGCGGCGATGTTGTC
 CGGCACCGGATGATGGCGCCAGAACTGCACAGGCAGTAGGGCTGGTCGCCGCTACAACAG
 ^ ^
 556 SAC2, 566 DRD1,
 ValValAlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAsp
 602 GTCGTGGCAACCGATGCCCTCATGACCGGCTATACCGGCGACTTCGACTCGGTGATAGAC
 CAGCACCGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTG
 ^
 621 BSPH1,
 CysAsnThrCysValThrGlnThrValAspPheSerLeuAspProThrPheThrIleGlu

FIGURE 11 - Page 2

662 TGCAATACGTGTGTACCCAGACAGTCGATTTTCAGCCTTGACCCTACCTTCACCATTGAG
ACGTTATGCACACAGTGGGTCTGTCTAGCTAAAGTCGGAAGTGGGATGGAAGTGGTAACTC

ThrIleThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArg
722 ACAATCACGCTCCCCAAGATGCTGTCTCCCGCACTCAACGTCGGGGCAGGACTGGCAGG
TGTTAGTGCGAGGGGGTTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCTGACCGTCC

GlyLysProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAsp
782 GGGAAAGCCAGGCATCTACAGATTTGTGGCACCAGGGGAGCGCCCCCTCCGGCATGTTTCGAC
CCCTTCGGTCCGTAGATGTCTAAACACCGTGGCCCCCTCGCGGGGAGGCCGTACAAGCTG

822 BGLI, 839 DRD1,

SerSerValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAla
842 TCGTCCGTCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTACGCCCCGC
AGCAGGCAGGAGACACTCACGATACTGCGTCCGACACGAACCATACTCGAGTGCGGGCGG

887 SACI,

GluThrThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAsp
902 GAGACTACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGAC
CTCTGATGTCAATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCTCTG

937 SMAI XMAI,

HisLeuGluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeu
962 CATCTTGAATTTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTA
GTAGAACTTAAACCCCTCCCGCAGAAATGTCCGGAGTGAGTATATCTACGGGTGAAAGAT

991 STUI,

SerGlnThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrVal
1022 TCCCAGACAAAGCAGAGTGGGAGAACCTTCCTTACCTGGTAGCGTACCAAGCCACCGTG
AGGGTCTGTTTCGTCTCACCCCTCTTGAAGGAATGGACCATCGCATGGTTCGGTGGCAC

1075 DRA3,

CysAlaArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArg
1082 TGCGCTAGGGCTCAAGCCCCCTCCCCATCGTGGGACCAGATGTGGAAGTGTGTTGATTGCG
ACGCGATCCCGAGTTCGGGGAGGGGGTAGCACCTGGTCTACACCTTCACAAACTAAGCG

LeuLysProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsn
1142 CTCAAGCCCACCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTTCAAGAT
GAGTTCGGGTGGGAGGTACCCGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTA

1156 NCOI,

GluIleThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeu
1202 GAAATCACCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTG
CTTTAGTGGGACTGCGTGGGTGAGTGGTTTATGTAGTACTGTACGTACAGCCGGCTGGAC

1236 BSPH1, 1240 DRD1, 1243 AVA3, 1251 EAG1 XMA3, 1256 DRD1,

GluValValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyr
1262 GAGGTCGTACGAGCACCTGGGTGCTCGTTGGCGGCGTCTGGCTGCTTTGGCCGCGTAT
CTCCAGCAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATA

FIGURE 11 - Page 3

CysLeuSerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAla
 1322 TGCCTGTCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCCGGAAGCCGGCA
 ACGGACAGTTGTCCGACGCACCAGTATCACCCGTCCCAGCAGAACAGGCCCTTCGGCCGT
 1375 NAEI,
 IleIleProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGln
 1382 ATCATACCTGACAGGGAAGTCCTCTACCGAGAGTTTCGATGAGATGGAAGAGTGCTCTCAG
 TAGTATGGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCAGAGAGTC
 1391 DRD1,
 HisLeuProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeu
 1442 CACTTACCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAAGCAGAAGGCCCTC
 GTGAATGGCATGTAGCTCGTTCCCTACTACGAGCGGCTCGTCAAGTTCGTCTCCGGGAG
 GlyLeuLeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsn
 1502 GGCCTCCTGCAGACCGCTCCCGTCAGGCAGAGGTTATCGCCCTGCTGTCCAGACCAAC
 CCGGAGGACGTCTGGCGCAGGGCAGTCCGTCTCCAATAGCGGGGACGACAGGTCTGGTTG
 1508 PSTI, 1513 TTH3I,
 TrpGlnLysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGln
 1562 TGGCAAAACTCGAGACCTTCTGGGCGAAGCATATGTGGAACCTTCATCAGTGGGATACAA
 ACCGTTTTTGAGCTCTGGAAGACCCGCTTCGTATACACCTTGAAGTAGTCACCCTATGTT
 1571 XHOI, 1592 NDEI,
 TyrLeuAlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPhe
 1622 TACTTGGCGGGCTTGTCAACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTT
 ATGAACCGCCCGAACAGTTGCGACGGACCATTTGGGGCGGTAACGAAGTAACCTACCGAAAA
 1649 BSTE2,
 ThrAlaAlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGly
 1682 ACAGCTGCTGTCAACAGCCCACTAACCCTAGCCAAACCCCTCTTCAACATATTGGGG
 TGTGACGACAGTGGTGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCC
 1683 ALWN1 PVU2,
 GlyTrpValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGly
 1742 GGGTGGGTGGCTGCCAGCTCGCCGCCCCCGGTGCCGCTACTGCCTTTGTGGGCGCTGGC
 CCCACCCACCGACGGGTCGAGCGGCGGGGGCCACGGCGATGACGGAAACCCCGCAGCG
 1800 ESP1,
 LeuAlaGlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAla
 1802 TTAGCTGGCGCCCATCGGCAGTGTGGACTGGGAAGGTCCTCATAGACATCCTTGCA
 AATCGACCGCGGGGTAGCCGTCACAACCTGACCCCTCCAGGAGTATCTGTAGGAACGT
 1808 KAS1 NARI,
 GlyTyrGlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluVal
 1862 GGGTATGGCGGGGCGTGGCGGGAGCTCTTGTGGCATTCAAGATCATGAGCGGTGAGGTC
 CCCATACCGCGCCCGCACC GCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAG

FIGURE 11 - Page 4

1884 SACI, 1905 BSPH1,

1922 ProSerThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuVal
 CCCTCCACGGAGGACCTGGTCAATCTACTGCCCGCCATCCTCTCGCCCGAGCCCTCGTA
 GGGAGGTGCCTCCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGGCCTCGGGAGCAT
 ^

1934 TTH3I,

1982 ValGlyValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaVal
 GTCGGCGTGGTCTGTGCAGCAATACTGCGCCGGCACGTTGGCCCGGCGAGGGGGCAGTG
 CAGCCGCACACAGACGTCGTTATGACGCGGCCGTGCAACCGGGCCCGCTCCCCCGTCAC
 ^

2010 NAEI, 2023 SMAI XMAI,

2042 GlnTrpMetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHis
 CAGTGGATGAACCGGCTGATAGCCTTCGCCTCCCGGGGAACCATGTTCCCCACGCAC
 GTCACCTACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGGTGCCTG
 ^

2073 SMAI XMAI, 2099 DRA3,

2102 TyrValProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrVal
 TACGTGCCGGAGAGCGATGCAGCTGCCGCGTCACTGCCATACTCAGCAGCCTCACTGTA
 ATGCACGGCCTCTCGCTACGTGACGGGCGCAGTGACGGTATGAGTCGTGAGGTGACAT
 ^

2121 PVU2,

2162 ThrGlnLeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSer
 ACCCAGCTCCTGAGGCGACTGCACCACTGGATAAGCTCGGAGTGTAACCACTCCATGCTCC
 TGGGTGCGAGGACTCCGCTGACGTGGTCACCTATTCGAGCCTCACATGGTGAGGTACGAGG
 ^

2165 ALWN1, 2170 MST2,

2222 GlySerTrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThr
 GGTTCCTGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACC
 CCAAGGACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGG
 ^

2226 ECON1,

2282 TrpLeuLysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArg
 TGGCTAAAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCCTTTGTGTCTGCCAGCGC
 ACCGATTTTTCGATTGAGTACGGTGTGACGGACCCTAGGGGAAACACAGGACGGTCGCG
 ^

2291 ESP1, 2306 PVU2, 2316 BAMHI,

2342 GlyTyrLysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAla
 GGGTATAAGGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGTGGCACTGTGGAGCT
 CCCATATTCCCCCAGACCGCTCCCCTGCCGTAGTACGTGTGAGCGACGGTGACACCTCGA
 ^

2402 GluIleThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArg
 GAGATCACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCCTAGGACCTGCAGG
 CTCTAGTGACCTGTACAGTTTTTGCCCTGCTACTCCTAGCAGCCAGGATCCTGGACGTCC
 ^

2431 BSAB1, 2447 AVR2, 2454 SSE83871, 2455 PSTI,

2462 AsnMetTrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeu
 AACATGTGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGGCCCTGTACCCCCCTT
 TTGTACACCTCACCTGGAAGGGGTAATTACGGATGTGGTGCCCGGGGACATGGGGGGAA
 ^

FIGURE 11 - Page 5

2486 ASE1, 2503 APAI,

2522 ProAlaProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIle
 CCTGCGCCGAACCTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATA
 GGACGCGGCTTGATGTGCAAGCGGATACCTCCCACAGACGTCTCCTTATGCACCTCTAT

2559 PSTI,

2582 ArgGlnValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysPro
 AGGCAGGTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCCG
 TCCGTCCACCCCTGAAGGTGATGCACTGCCATACTGATGACTGTTAGAATTTACGGGC

2600 DRA3,

2642 CysGlnValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPhe
 TGCCAGGTCCCATCGCCCAATTTTTCACAGAATTGGACGGGGTGCCTACATAGGTTT
 ACGGTCCAGGTAGCGGGCTTAAAAAGTGTCTTAACCTGCCCCACGGGATGTATCCAA

2702 AlaProProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGlu
 GCGCCCCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTCAGAGTAGGACTCCACGAA
 CGCGGGGGACGTTGCGGAACGACGCCCTCCTCCATAGTAAGTCTCATCCTGAGGTGCTT

2762 TyrProValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSer
 TACCCGGTAGGGTCGCAATTACCTTGCAGCCCGAACCGACGTGGCCGTGTTGACGTCC
 ATGGGCCATCCAGCGTTAATGGAACGCTCGGGCTTGGCCTGCACCGGCACAACCTGCAGG

2763 HGIE2, 2815 AAT2,

2822 MetLeuThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGly
 ATGCTCACTGATCCCTCCCATATAACAGCAGAGGCGGCCGGCGAAGGTTGGCGAGGGGA
 TACGAGTGACTAGGGAGGGTATATTGTCGTCTCCGCCGGCCCGCTTCCAACCGCTCCCTT

2856 EAG1 XMA3,

2882 SerProProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAla
 TCACCCCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCA
 AGTGGGGGAGACACCGGTCGAGGAGCCGATCGGTCGATAGGCGAGGTAGAGAGTTCGCT

2895 BALI, 2909 NHEI,

2942 ThrCysThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrp
 ACTTGACCGCTAACCATGACTCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGG
 TGAACGTGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGTTTGGAGGATACC

2972 ESP1, 2975 SACI,

3002 ArgGlnGluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeu
 AGGCAGGAGATGGGCGGCAACATCACCAGGGTTGAGTCAGAAAACAAAGTGGTGATTCTG
 TCCGTCTCTACCCGCCGTTGTAGTGGTCCCAACTCAGTCTTTGTTTACCACTAAGAC

3062 AspSerPheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGlu
 GACTCCTTCGATCCGCTTGTGGCGGAGGAGACGAGCGGGAGATCTCCGTACCCGCAGAA
 CTGAGGAAGCTAGGCGAACACCGCCTCCTCCTGCTCGCCCTCTAGAGGCATGGGCGTCTT

3102 BGL2,

FIGURE 11 - Page 6

IleLeuArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyr
 3122 ATCCTGCGGAAGTCTCGGAGATTGCCCCAGGCCCTGCCGTTTGGGCGGGCCGGACTAT
 TAGGACGCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGGCCTGATA
 3149 ALWN1, 3170 EAG1 XMA3,
 AsnProProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGly
 3182 AACCCCCCGCTAGTGGAGACGTGGAAAAAGCCCGACTACGAACCACCTGTGGTCCATGGC
 TTGGGGGGCGATCACCTCTGCACCTTTTTCGGGCTGATGCTTGGTGGACACCAGGTACCG
 3223 HGIE2, 3235 NCOI,
 CysProLeuProProProLysSerProProValProProProArgLysLysArgThrVal
 3242 TGCCCGCTTCCACCTCCAAAGTCCCTCCTGTGCCTCCGCTCGGAAGAAGCGGACGGTG
 ACGGGCGAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTTCGCCTGCCAC
 ValLeuThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGly
 3302 GTCCTCACTGAATCAACCCTATCTACTGCCTTGCCCGAGCTCGCCACCAGAAGCTTTGGC
 CAGGAGTGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCG
 3338 SACI, 3352 HIND3,
 SerSerSerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaPro
 3362 AGCTCCTCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCT
 TCGAGGAGTTGAAGGCCGTAATGCCCCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGA
 SerGlyCysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGly
 3422 TCTGGCTGCCCCCGACTCCGACGCTGAGTCTTATCCTCCATGCCCCCCTGGAGGGG
 AGACCGACGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCC
 3443 EAM11051,
 GluProGlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsn
 3482 GAGCCTGGGGATCCGGATCTTAGCGACGGGTATGGTCAACGGTCAGTAGTGAGGCCAAC
 CTCGGACCCCTAGGCCTAGAATCGCTGCCAGTACCAGTTGCCAGTCATCACTCCGGTTG
 3490 BAMHI, 3491 BSAB1, 3493 BSPE1,
 AlaGluAspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrPro
 3542 GCGGAGGATGTCGTGTGCTGCTCAATGTCTTACTCTTGGACAGGCGCACTCGTCACCCCCG
 CGCCTCCTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCGCGTGAGCAGTGGGGC
 3595 DRA3,
 CysAlaAlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHis
 3602 TGCGCCGCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTCAC
 ACGCGCGCCTTCTTGTCTTTGACGGGTAGTTACGTGATTCTGTTGAGCAACGATGCAGTG
 3606 SAC2, 3617 ALWN1, 3661 PFLM1,
 HisAsnLeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThr
 3662 CACAATTTGGTGTATTCCACCACCTCACGCAGTGCTTGCCAAAGGCAGAAGAAAGTCACA
 GTGTTAAACCACATAAGGTGGTGGAGTGCGTCACGAACGGTTCCGTCTTCTTTCAGTGT
 3687 DRA3,
 PheAspArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAla

FIGURE 11 - Page 7

3722 TTTGACAGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCA
AAACTGTCTGACGTTCAAGACCTGTCGGTAATGGTCCTGCATGAGTTCCTCCAATTCGT

AlaAlaSerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrPro
3782 GCGGCGTCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGACGCTGACGCCC
CGCCGCAGTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTCGGACTGCGGG
^

3822 HIND3,

ProHisSerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArg
3842 CCACACTCAGCCAAATCCAAGTTTGGTTATGGGGCAAAAGACGTCCGTTGCCATGCCAGA
GGTGTGAGTCGGTTTAGGTTCAAACCAATACCCCGTTTCTGCAGGCAACGGTACGGTCT
^

3881 AAT2, 3896 BGLI,

LysAlaValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrPro
3902 AAGGCCGTAAACCACATCAACTCCGTGTGGAAGACCTTCTGGAAGACAATGTAACACCA
TTCCGGCATTGGGTGTAGTTGAGGCACACCTTCTGGAAGACCTTCTGTTACATTGTGGT

IleAspThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGly
3962 ATAGACACTACCATCATGGCTAAGAACGAGGTTTTCTGCGTTTACGCTGAGAAGGGGGGT
TATCTGTGATGGTAGTACCGATTCTTGCTCCAAAGACGCAAGTCGGACTCTTCCCCCA

ArgLysProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMet
4022 CGTAAGCCAGCTCGTCTCATCGTGTTCCTCCGATCTGGGCGTGCGGTGTGCGAAAAGATG
GCATTCCGTCGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACACGCTTTCTAC

AlaLeuTyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPhe
4082 GCTTTGTACGACGTGTTACAAAGCTCCCTTGGCCGTGATGGGAAGCTCCTACGGATT
CGAAACATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCCTTCGAGGATGCCTAAG

GlnTyrSerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThr
4142 CAATACTCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGGAAGTCCAAGAAAACC
GTTATGAGTGGTCTGTCGCCAACTTAAGGAGCACGTTTCGCACCTCAGGTTCTTTTGG
^

4166 ECORI,

ProMetGlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIle
4202 CCAATGGGGTTCTCGTATGATACCCGCTGCTTTGACTCCACAGTCACTGAGAGCGACATC
GGTTACCCCAAGAGCATACTATGGGCGACGAAACTGAGGTGTCAGTGACTCTCGCTGTAG
^

4235 DRD1, 4242 ALWN1,

ArgThrGluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIle
4262 CGTACGGAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCCAAGCCCGGTGGCCATC
GCATGCCTCCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTCCGGCGCACCGGTAG
^

4307 BGLI, 4314 BALI,

LysSerLeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsn
4322 AAGTCCCTCACCAGAGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAAC
TTCAGGAGTGGCTCTCCGAAATACAACCCCGGGAGAATGGTTAAGTCCCCCTCTTG
^

4351 APAI,

CysGlyTyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeu
4382 TGCGGCTATCGCAGGTGCCGCGAGCGCGTACTGACAACTAGCTGTGGTAACACCTCT

FIGURE 11 - Page 8

ACGCCGATAGCGTCCACGGCGCGCTCGCCGCATGACTGTTGATCGACACCATTGTGGGAG
4442 ThrCysTyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMet
ACTTGCTACATCAAGGCCCGGGCAGCCTGTCGAGCCGAGGGCTCCAGGACTGCACCATG
TGAACGATGTAGTTCCGGGCCCGTCCGGACAGCTCGGCGTCCCGAGGTCCTGACGTGGTAC
4458 SMAI XMAI,
4502 LeuValCysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAla
CTCGTGTGTGGCGACGACTTAGTCGTTATCTGTGAAAGCGCGGGGTCCAGGAGGACGCG
GAGCACACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCCTCTCGCG
4514 DRD1, 4517 TTH3I,
4562 AlaSerLeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspPro
GCGAGCCTGAGAGCCTTCACGGAGGCTATGACCAGGTACTCCGCCCCCCTGGGGACCCC
CGCTCGGACTCTCGGAAGTGCTCCGATACTGGTCCATGAGGCGGGGGGACCCCTGGGG
4622 ProGlnProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAla
CCACAACAGAATACGACTTGGAGCTCATAACATCATGCTCTCCAACGTGTCAGTCGCC
GGTGTGGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGG
4643 SACI,
4682 HisAspGlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAla
CACGACGGCGCTGGAAAGAGGGTCTACTACCTCACCCGTGACCCTACAACCCCCCTCGCG
GTGCTGCCGCGACCTTCTCCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGGAGCGG
4737 NRUI,
4742 ArgAlaAlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIle
AGAGCTGCGTGGGAGACAGCAAGACACACTCCAGTCAATTCCTGGCTAGGCAACATAATC
TCTCGACGCACCCTCTGTCGTTCTGTGTGAGGTCAGTTAAGGACCGATCCGTTGTATTAG
4802 MetPheAlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeu
ATGTTTGGCCCCACACTGTGGGCGAGGATGATACTGATGACCCATTTCTTTAGCGTCCTT
TACAAACGGGGGTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAA
4812 PFLM1, 4813 DRA3,
4862 IleAlaArgAspGlnLeuGluGlnAlaLeuAspCysGluIleTyrGlyAlaCysTyrSer
ATAGCCAGGGACCAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCCTGCTACTCC
TATCGGTCCCTGGTCGAACCTGTCCGGGAGCTAACGCTCTAGATGCCCCGACGATGAGG
4899 BGL2,
4922 IleGluProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSer
ATAGAACCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTTCA
TATCTTGGTGACCTAGATGGAGGTTAGTAAGTTTCTGAGGTACCGGAGTCGCGTAAAAGT
4960 NCOI,
4982 LeuHisSerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGly
CTCCACAGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGCATGCCTCAGAAAACCTGGG
GAGGTGTCAATGAGAGGTCCACTTTAGTTATCCACCGGCGTACGGAGTCTTTTGAACCC
5021 SPHI, 5041 KPNI,

FIGURE 11 - Page 9

ValProProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAla
 5042 GTACCGCCCTTGCGAGCTTGAGACACCGGGCCCGGAGCGTCCGCGCTAGGCTTCTGGCC
 CATGGCGGGAACGCTCGAACCTCTGTGGCCCGGGCCTCGCAGGCGCGATCCGAAGACCGG
 5070 APAI, 5097 BALI,
 ArgGlyGlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLys
 5102 AGAGGAGGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAG
 TCTCCTCCGTCCCACGGTATACACCGTTTCATGGAGAAGTTGACCCGTCATTCTTGTTTC
 5119 NDEI,
 LeuLysLeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAla
 5162 CTCAAACCTCACTCCAATAGCGGCCGCTGGCCAGCTGGACTTGTCCGGCTGGTTCACGGCT
 GAGTTTGAGTGAGGTTATCGCCGGCGACCGGTGACCTGAACAGGCCGACCAAGTGCCGA
 5180 NOTI, 5181 EAGI XMA3, 5188 BALI, 5192 PVU2,
 GlyTyrSerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrp
 5222 GGCTACAGCGGGGAGACATTTATCACAGCGTGTCTCATGCCCGGCCCGCTGGATCTGG
 CCGATGTCGCCCCCTCTGTAAATAGTGTGCGCACAGAGTACGGGCCGGGGCGACCTAGACC
 5246 DRA3,
 PheCysLeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgOP
 5282 TTTTGCCTACTCCTGCTTGCTGCAGGGGTAGGCATCTACCTCCTCCCAACCGATGAAGG
 AAAACGGATGAGGACGAACGACGTCCCATCCGTAGATGGAGGAGGGGTTGGCTACTTCC
 5301 PSTI, 5331 HGIE2,
 TTGGGGTAAACACTCCGGCCTAAAAAAAAAAAAAAAAATCTAGAACCCGAGTCGAC
 5342 AACCCCATTTGTGAGGCCGATTTTTTTTTTTTTTTAGATCTTGGGCTCAGCTG
 5378 XBAI, 5390 SALI,

FIGURE 12

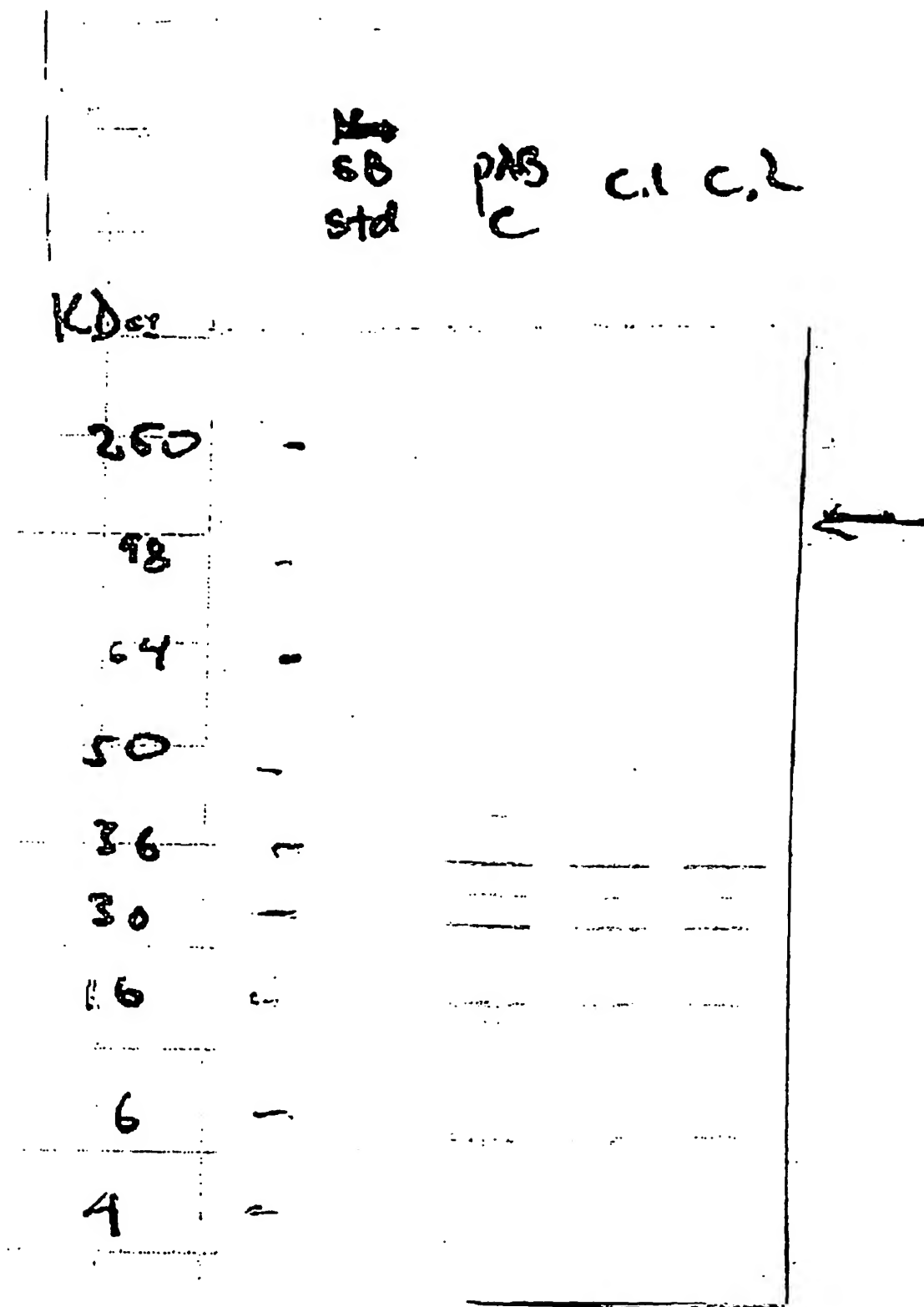


FIGURE 13

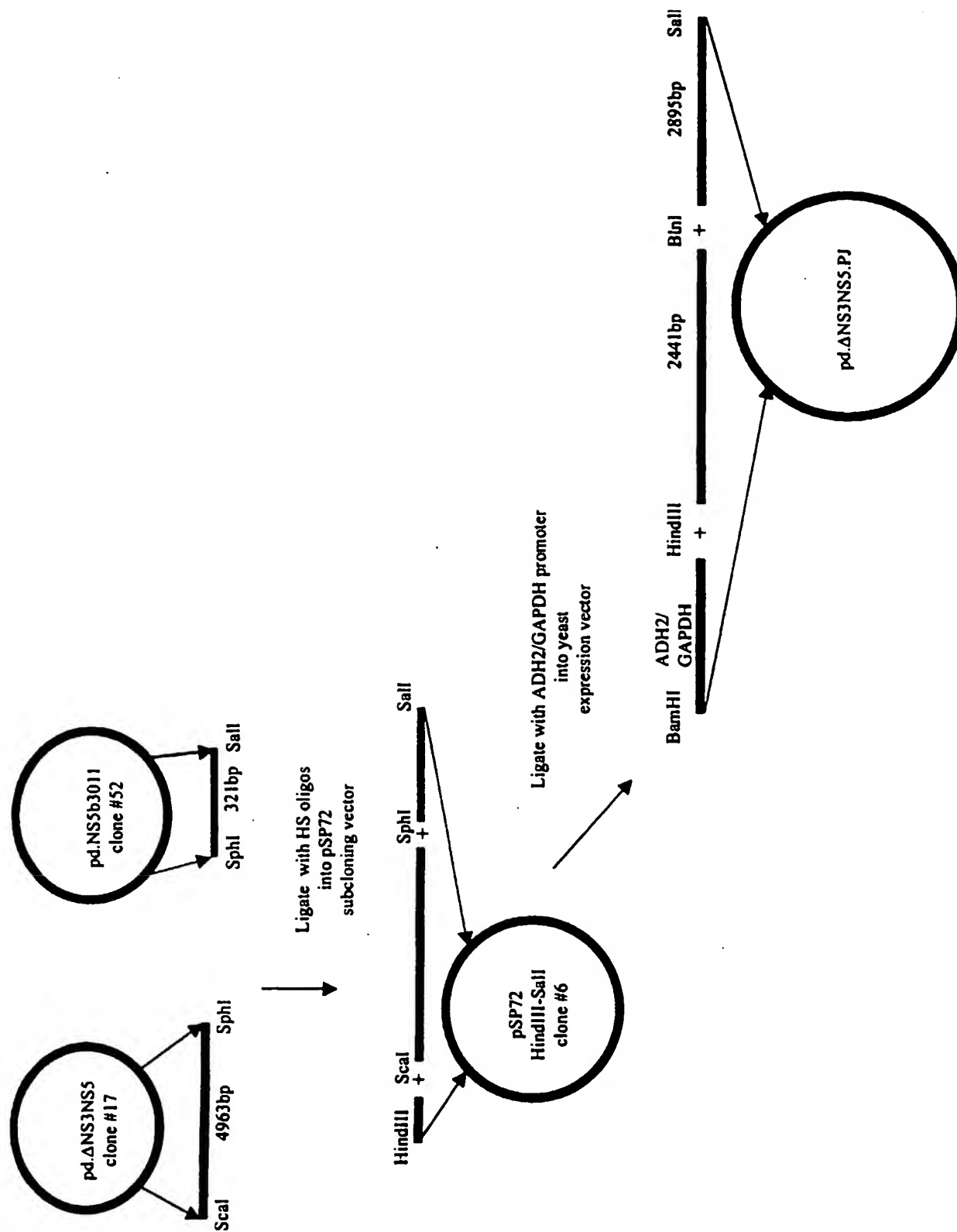


FIGURE 14 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuValLeuAsn
 2 AGCTTACAAAACAAAATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTACTCAAC
 TCGAATGTTTTGTTTTACCGACGTATACGTCGAGTCCCGATATTCCACGATCATGAGTTG
 ^ ^
 1 HIND3, 24 NDEI, 52 SCAI,
 ProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGlyIleAsp
 62 CCCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGGATCGAT
 GGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCCTAGCTA
 ^
 116 CLAI,
 ProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyrSerThr
 122 CCTAACATCAGGACCGGGGTGAGAACAATTACCACTGGCAGCCCCATCACGTACTCCACC
 GGATTGTAGTCCTGGCCCCACTCTTGTTAATGGTGACCGTCGGGGTAGTGCATGAGGTGG
 TyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIleIleCys
 182 TACGGCAAGTTCCTTGCCGACGCGGGTGCTCGGGGGGCGCTTATGACATAATAATTTGT
 ATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGCAATACTGTATTATTAAACA
 AspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeuAspGln
 242 GACGAGTGCCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGTCCTTGACCAA
 CTGCTCACGGTGAGGTGCCTACGGTGTAGGTAGAACCCGTAACCGTGACAGGAACCTGGTT
 AlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGlySerVal
 302 GCAGAGACTGCGGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGCTCCGTC
 CGTCTCTGACGCCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGGAGGCCGAGGCAG
 ^
 303 ALWN1,
 ThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIleProPhe
 362 ACTGTGCCCCATCCCAACATCGAGGAGTTGCTCTGTCCACCACCGGAGAGATCCCTTTT
 TGACACGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAGGGA
 TyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePheCysHis
 422 TACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTCTGTCAT
 ATGCCGTTCCGATAGGGGGAGCTTCATTAGTTCCCCCCTCTGTAGAGTAGAAGACAGTA
 SerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsnAlaVal
 482 TCAAAGAAGAAGTGCGACGAACTCGCCGCAAAGCTGGTCGCATTGGGCATCAATGCCGTG
 AGTTTCTTCTTACGCTGCTTGAGCGGCGTTTCGACCAGCGTAACCCGTAGTTACGGCAC
 AlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValValValVal
 542 GCCTACTACCGGGTCTTGACGTGTCCGTATCCCGACCAGCGCGATGTTGTGCTGCTG
 CGGATGATGGCGCCAGAACTGCACAGGCAGTAGGGCTGGTCGCGCTACAACAGCAGCAC
 ^ ^
 550 SAC2, 560 DRD1,
 AlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAspCysAsn
 602 GCAACCGATGCCCTCATGACCGGCTATACCGGCGACTTCGACTCGGTGATAGACTGCAAT
 CGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTGACGTTA
 ^
 615 BSPH1.

FIGURE 14 - Page 2

662 ACGTGTGTACCCAGACAGTCGATTTTCAGCCTTGACCCTACCTTCACCATTTGAGACAATC
 TGCACACAGTGGGTCTGTAGCTAAAGTCGGAAGTGGGATGGAAGTGGTAACTCTGTTAG
 ThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArgGlyLys
 722 ACGTCCCCCAAGATGCTGTCTCCCGCACTCAACGTCGGGGCAGGACTGGCAGGGGGAAG
 TGCAGGGGGTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCTGACCGTCCCCCTTC
 ProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAspSerSer
 782 CCAGGCATCTACAGATTTGTGGCACCAGGGGAGCGCCCCCTCCGGCATGTTGCACTCGTCC
 GGTCCGTAGATGTCTAACACCGTGGCCCCCTCGCGGGGAGGCGGTACAAGCTGAGCAGG
 816 BGLI, 833 DRD1,
 ValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAlaGluThr
 842 GTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTCACGCCCGCCGAGACT
 CAGGAGACACTCACGATACTGCGTCCGACACGAACCATACTCGAGTGCGGGCGGCTCTGA
 881 SACI,
 ThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAspHisLeu
 902 ACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGACCATCTT
 TGTCAATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCTGGTAGAA
 931 SMAI XMAI,
 GluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeuSerGln
 962 GAATTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTATCCCAG
 CTTAAACCCCTCCCGCAGAAATGTCCGGAGTGAGTATATCTACGGGTGAAAGATAGGGTC
 985 STUI,
 ThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrValCysAla
 1022 ACAAGCAGAGTGGGGAGAACCTTCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCT
 TGTTTCGTCTACCCCTCTTGAAGGAATGGACCATCGCATGGTTTCGGTGGCACACGCCA
 1069 DRA3,
 ArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArgLeuLys
 1082 AGGGCTCAAGCCCCTCCCCATCGTGGGACCAGATGTGGAAGTGTGTTGATTGCGCTCAAG
 TCCCGAGTTCGGGGAGGGGTAGCACCCCTGGTCTACACCTTCACAACTAAGCGGAGTTC
 ProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsnGluIle
 1142 CCCACCCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTGAGAATGAAATC
 GGGTGGGAGGTACCCGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTACTTTAG
 1150 NCOI,
 ThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeuGluVal
 1202 ACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTGGAGGTC
 TGGGACTGCGTGGGTGAGTGGTTTATGTAGTACTGTACGTACAGCCGCTGGACCTCCAG
 1230 BSPH1, 1234 DRD1, 1237 AVA3, 1245 EAG1 XMA3, 1250 DRD1,
 ValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyrCysLeu
 1262 GTACGAGCACCTGGGTGCTCGTTGGCGGCGTCTGGCTGCTTTGGCCGCGTATTGCGCTG
 CAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATAACGGAC

FIGURE 14 - Page 3

SerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAlaIleIle
 1322 TCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCGGGAAGCCGGCAATCATA
 AGTTGTCCGACGCACCAGTATCACCCGTCCAGCAGAACAGGCCCTTCGGCCGTTAGTAT
 1369 NAEI,

ProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGlnHisLeu
 1382 CCTGACAGGGAAGTCCTCTACCGAGAGTTCGATGAGATGGAAGAGTGCTCTCAGCACTTA
 GGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCACGAGAGTCGTGAAT
 1385 DRD1,

ProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeuGlyLeu
 1442 CCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAAGCAGAAGGCCCTCGGCCTC
 GGCATGTAGCTCGTTCCTACTACGAGCGGCTCGTCAAGTTCGTCTTCGGGAGCCGGAG
 LeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsnTrpGln
 1502 CTGCAGACCGCGTCCCGTCAGGCAGAGGTTATCGCCCCTGCTGTCCAGACCAACTGGCAA
 GACGTCTGGCGCAGGGCAGTCCGTCTCCAATAGCGGGGACGACAGGTCTGGTTGACCGTT
 1502 PSTI, 1507 TTH3I,

LysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGlnTyrLeu
 1562 AAACCTCGAGACCTTCTGGGCGAAGCATATGTGGAACCTTCATCAGTGGGATACAATACTTG
 TTTGAGCTCTGGAAGACCCGCTTCGTATACACCTTGAAGTAGTCACCCTATGTTATGAAC
 1565 XHOI, 1586 NDEI,

AlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPheThrAla
 1622 GCGGGCTTGTCACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTTACAGCT
 CGCCCGAACAGTTGCGACGGACCATTTGGGGCGGTAACGAAGTAACTACCGAAAATGTCTGA
 1643 BSTE2, 1677 ALWN1 PVU2,

AlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGlyGlyTrp
 1682 GCTGTCAACAGCCCACTAACCCTAGCCAAACCCCTCCTCTTCAACATATTGGGGGGGTGG
 CGACAGTGGTGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCCCCCACC
 ValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGlyLeuAla
 1742 GTGGCTGCCAGCTCGCCGCCCCCGGTGCCGCTACTGCCTTTGTGGGCGCTGGCTTAGCT
 CACCGACGGTTCGAGCGGCGGGGGCCACGGCGATGACGGAACACCCGCGACCGAATCGA
 1794 ESI1,

GlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAlaGlyTyr
 1802 GGCGCCGCCATCGGCAGTGTGGACTGGGGAAGGTCTCATAGACATCCTTGCAAGGTAT
 CCGCGGCGGTAGCCGTCACAACCTGACCCCTTCCAGGAGTATCTGTAGGAACGTCCCAT
 1802 KAS1 NARI,

GlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluValProSer
 1862 GGCGCGGGCGTGGCGGGAGCTCTTGTTGGCATTCAAGATCATGAGCGGTGAGGTCCCTCC
 CCGCGCCCGCACCGCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAGGGGAGG
 1878 SACI, 1899 BSPH1,

FIGURE 14 - Page 4

ThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuValValGly
 1922 ACGGAGGACCTGGTCAATCTACTGCCCCCATCTCTCGCCCGGAGCCCTCCTAGTCGGC
 TGCCTCCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGSCCTCGGGAGCATCAGCCG
 ^
 1928 TTH3I,
 ValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaValGlnTrp
 1982 GTGGTCTGTGCAGCAATACTGCGCCGGCACGTTGGCCCGGGGAGGGGGCAGTGCACTGG
 CACCAGACACGTCGTTATGACGCGGCCGTGCAACCGGGCCGCTCCCCCGTCACGTCACC
 ^
 2004 NAEI, 2017 SMAI XMAI,
 MetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal
 2042 ATGAACCGGCTGATAGCCTTCGCCTCCCGGGGGAACCATGTTTCCCCCAGCCTACGTC
 TACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGGTGCGTGATGCAC
 ^
 2067 SMAI XMAI, 2093 DRA3,
 ProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrValThrGln
 2102 CCGGAGAGCGATGCAGCTGCCCGCGTCACTGCCATACTCAGCAGCCTCACTGTAAACCCAG
 GGCTCTCGCTACGTCGACGGGCGCAGTGACGGTATGAGTCGTCGGAGTGACATTGGGTC
 ^
 2115 PVU2, 2159 ALWN1,
 LeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSerGlySer
 2162 CTCCTGAGGCGACTGCACCAGTGGATAAGCTCGGAGTGTACCACTCCATGCTCCGGTTC
 GAGGACTCCGCTGACGTGGTCACCTATTCGAGCCTCACATGGTGAGGTACGAGGCCAAGG
 ^
 2164 MST2, 2220 ECON1,
 TrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThrTrpLeu
 2222 TGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACCTGGCTA
 ACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGGACCGAT
 ^
 LysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArgGlyTyr
 2292 AAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCCCTTGTGTCTGCCAGCGCGGGTAT
 TTTGATTTCGAGTACGGTGTGACGGACCCTAGGGGAAACACAGGACGGTCGCGCCCAT
 ^
 2285 ESP1, 2300 PVU2, 2310 BAMHI,
 LysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAlaGluIle
 2342 AAGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGCTGCCACTGTGGAGCTGAGATC
 TTCCCCCAGACCGCTCCCTGCCGTAGTACGTGTGAGCGACGGTGACACCTCGACTCTAG
 ^
 ThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArgAsnMet
 2402 ACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCTAGGACCTGCAGGAACATG
 TGACCTGTACAGTTTTTGCCTGTACTCCTAGCAGCCAGGATCCTGGACGTCCTTGATC
 ^
 2425 BSAB1, 2441 AVR2, 2448 SSE83871, 2449 PSTI,
 TrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeuProAla
 2462 TGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGCCCCCTGTACCCCCCTTCTGCG
 ACCTCACCTGGAAGGGTAATTACGGATGTGGTGCCCGGGGACATGGGGGAAGGACGC
 ^
 2480 ASE1, 2497 APAI,
 ProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIleArgGln

FIGURE 14 - Page 5

2522 CCGAACTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATAAGGCAG
 GGCTTGATGTGCAAGCGCGATACCTCCACAGACGTCTCCTTATGCACCTCTATTCCGTC
 2553 PSTI,
 ValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysProCysGln
 2582 GTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCGTGCCAG
 CACCCCTGAAGGTGATGCACTGCCCATACTGATGACTGTTAGAATTTACGGGCACGGTC
 2594 DRA3,
 ValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPheAlaPro
 2642 GTCCCATCGCCGAATTTTTCACAGAATTGGACGGGGTGCGCCTACATAGGTTTGCGCC
 CAGGGTAGCGGGCTTAAAAAGTGTCTTAACCTGCCCCACGCGGATGTATCCAAACGCGGG
 ProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGluTyrPro
 2702 CCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTAGAGTAGGACTCCACGAATACCCG
 GGGACGTTGCGGAACGACGCCCTCCTCCATAGTAAGTCTCATCCTGAGGTGCTTATGGGC
 2757 HGIE2,
 ValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSerMetLeu
 2762 GTAGGGTCGCAATTACCTTGCGAGCCCGAACCGGACGTGGCCGTGTTGACGTCCATGCTC
 CATCCACGCGTTAATGGAACGCTCGGGCTTGGCCTGCACCGGCACAACCTGCAGGTACGAG
 2809 AAT2,
 ThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGlySerPro
 2922 ACTGATCCCTCCCATATAACAGCAGAGCGCGCGCGGCGAAGGTTGGCGAGGGGATCACCC
 TGACTAGGGAGGGTATATTGTCGTCTCCGCGCGCGCGCTTCCAACCGTCCCTAGTGGG
 2850 EAG1 XMA3,
 ProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAlaThrCys
 2982 CCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCAACTTGC
 GGGAGACACCGGTCGAGGAGCCGATCGGTCGATAGGCGAGGTAGAGAGTTCCGTTGAACG
 2889 BALI, 2903 NHEI,
 ThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrpArgGln
 2942 ACCGTAACCATGACTCCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGGAGGCAG
 TGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGTTGGAGGATACCTCCGTC
 2966 ESP1, 2969 SACI,
 GluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeuAspSer
 3002 GAGATGGGCGGCAACATCACCAGGGTTGAGTCAGAAAACAAAGTGGTGATTCTGGACTCC
 CTCTACCCGCCGTTGTAGTGGTCCCAACTCAGTCTTTGTTTCACCACTAAGACCTGAGG
 PheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGluIleLeu
 3062 TTCGATCCGCTTGTGGCGGAGGAGGACGAGCGGGAGATCTCCGTACCCGAGAAATCCTG
 AAGCTAGGCGAACACCGCCTCCTCTGCTCGCCCTCTAGAGGCATGGGCGTCTTTAGGAC
 3096 BGL2,
 ArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyrAsnPro
 3122 CGGAAGTCTCGGAGATTCGCCAGGCCCTGCCGTTTGGGCGCGGCCGGACTATAACCCC

FIGURE 14 - Page 6

GCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGCCTGATATTGGGG
 3143 ALWN1, 3164 EAG1 XMA3,
 3182 ProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGlyCysPro
 CCGCTAGTGGAGACGTGGAAAAAGCCCGACTACGAACCACCTGTGGTCCATGGCTGCCCCG
 GCGCATCACCTCTGCACCTTTTTCGGGCTGATGCTTGGTGGACACCAGGTACCGACGGGG
 3217 HGIE2, 3229 NCOI,
 3242 LeuProProProLysSerProProValProProProArgLysLysArgThrValValLeu
 CTTCACCTCCAAAGTCCCCTCTGTGCCTCCGCCTCGGAAGAAGCGGACGGTGGTCTCTC
 GAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTTCGCCTGCCACCAGGAG
 3302 ThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGlySerSer
 ACTGAATCAACCCTATCTACTGCCTTGGCCGAGCTCGCCACCAGAAGCTTTGGCAGCTCC
 TGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCGTCGAGG
 3332 SACI, 3346 HIND3,
 3362 SerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaProSerGly
 TCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCTTCTGGC
 AGTTGAAGGCCGTAAATGCCCGCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGAAGACCG
 3422 CysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGlyGluPro
 TGCCCCCGGACTCCGACGCTGAGTCCTATTCTCCATGCCCCCCTGGAGGGGGAGCCT
 ACGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCCCTCGGA
 3437 EAM11051,
 3482 GlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsnAlaGlu
 GGGGATCCGGATCTTAGCGACGGGTCAAGGTCAGTAGTGGGCCAACGCGGAG
 CCCCTAGGCCTAGAATCGCTGCCCAGTACCAGTTGCCAGTCATCACTCCGGTTGCGCCTC
 3484 BAMHI, 3485 BSAB1, 3487 BSPE1,
 3542 AspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrProCysAla
 GATGTCGTGTGCTCAATGTCTTACTCTTGGACAGGCGCACTCGTCACCCCGTGCGCC
 CTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCGCGTGAGCAGTGGGGCACGCGG
 3589 DRA3, 3600 SAC2,
 3602 AlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHisHisAsn
 GCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTCACCACAAT
 CGCCTTCTTGTCTTTGACGGGTAGTTACGTGATTCTGTTGAGCAACGATGCAGTGGTGTTA
 3611 ALWN1, 3655 PFLM1,
 3662 LeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThrPheAsp
 TTGGTGTATTCCACCACCTCAGCAGTGCTTGCCAAAGGCAGAAGAAAGTCACATTTGAC
 AACCACATAAGGTGGTGGAGTGCGTCACGAACGGTTCCGTCTTCTTTCAGTGTAAGCTG
 3681 DRA3,
 3722 ArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAlaAlaAla
 AGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCAGCGGCG
 TCTGACGTTCAAGACCTGTCGGTAATGGTCTGCATGAGTTCCTCCAATTTCTGTCGCGCG

FIGURE 14 - Page 7

SerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrProProHis
 3782 TCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGACGCTGACGCCCCACAC
 AGTTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTCGGAAGTGCAGGGGGTGTG
 3816 HIND3,
 SerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArgLysAla
 3942 TCAGCCAAATCCAAGTTTGGTTATGGGGCAAAGACGTCCGTTGCCATGCCAGAAAGGCC
 AGTCGGTTTAGGTTCAAACCAATACCCCGTTTTCTGCAGGCAACGGTACGGTCTTTCCGG
 3875 AAT2, 3890 BGLI,
 ValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrProIleAsp
 3902 GTAACCCACATCAACTCCGTGTGGAAAGACCTTCTGGAAGACAATGTAACACCAATAGAC
 CATTGGGTGTAGTTGAGGCACACCTTTCTGGAAGACCTTCTGTTACATTGTGGTTATCTG
 ThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGlyArgLys
 3962 ACTACCATCATGGCTAAGAACGAGGTTTTCTGCGTTTCAGCCTGAGAAGGGGGTCTGAAG
 TGATGGTAGTACCGATTCTTGCTCCAAAAGACGCAAGTCGGAAGTCTTCCCCCAGCATTC
 ProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMetAlaLeu
 4022 CCAGCTCGTCTCATCGTGTTCCTCGATCTGGGCGTGCAGCGTGTGCGAAAAGATGGCTTTG
 GGTCGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACACGCTTTTCTACCGAAAC
 TyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPheGlnTyr
 4082 TACGACGTGGTTACAAAGCTCCCCTTGCCCGTGATGGGAAGCTCCTACGGATTCCAATAC
 ATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCTTCGAGGATGCCTAAGGTTATG
 SerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThrProMet
 4142 TCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGGAAGTCCAAGAAAACCCCAATG
 AGTGGTCTGTGCGCCCACTTAAGGAGCAGGTTTCGCACCTTCAGGTTCTTTGGGGTTAC
 4160 ECORI,
 GlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIleArgThr
 4202 GGGTTCTCGTATGATACCGCTGCTTTTGACTCCACAGTCACTGAGAGCGACATCCGTACG
 CCCAAGAGCATACTATGGGCGACGAACTGAGGTGTCAGTGACTCTCGCTGTAGGCATGC
 4229 DRD1, 4236 ALWN1,
 GluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIleLysSer
 4262 GAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCAAGCCCGCTGGCCATCAAGTCC
 CTCCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTTCGGGCGCACCGGTAGTTCAGG
 4301 BGLI, 4308 BALI,
 LeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsnCysGly
 4322 CTCACCGAGAGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAACTGCGGC
 GAGTGGCTCTCCGAAATACAACCCCGGAGAATGGTTAAGTTCCCCCTCTTGACGCCG
 4345 APAI,
 TyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeuThrCys
 4382 TATCGCAGGTGCCGCGCGAGCGGCGTACTGACAACCTAGCTGTGGTAACACCCTCACTTGC
 ATAGCGTCCACGGCGCGCTCGCCGCATGACTGTTGATCGACACCATTGTGGGAGTGAACG

FIGURE 14 - Page 8

TyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMetLeuVal
 4442 TACATCAAGGCCCGGGCAGCCTGTCGAGCCGAGGGCTCCAGGACTGCACCATGCTCGTG
 ATGTAGTTCGGGGCCGTCGGACAGCTCGGCCTCCCGAGGTCCTGACGTGGTACGAGCAC
 ^
 4452 SMAI XMAI,
 CysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAlaAlaSer
 4502 TGTGGCGACGACTTAGTTCGTTATCTGTGAAAGCGCGGGGGTCCAGGAGGACGCGGCGAGC
 ACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCCTCCTGCGCCGCTCG
 ^ ^
 4508 DRD1, 4511 TTH3I,
 LeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspProProGln
 4562 CTGAGAGCCTTCACGGAGGCTATGACCAGGTACTCCGCCCCCCTGGGGACCCCCACAA
 GACTCTCGGAAGTGCTCCGATACTGGTCCATGAGCGGGGGGGACCCCTGGGGGGTGTT
 ProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAlaHisAsp
 4622 CCAGAATACGACTTGGAGCTCATAACATCATGCTCCTCCAACGTGTCAGTCGCCCACGAC
 GGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGGGTGCTG
 ^
 4637 SACI,
 GlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAlaArgAla
 4682 GCGCTGGAAAGAGGGTCTACTACCTCACCCGTGACCCTACAACCCCCCTCGCGAGAGCT
 CCGCGACCTTTCTCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGAGCGCTCTCGA
 ^
 4731 NRUI,
 AlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIleMetPhe
 4742 GCGTGGGAGACAGCAAGACACACTCCAGTCAATTCCTGGCTAGGCAACATAATCATGTTT
 CGCACCTCTGTCTTCTGTGTGAGGTCAAGTAAAGACCGATCCGTTGTATTAGTACAAA
 AlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeuIleAla
 4802 GCCCCACACTGTGGGCGAGGATGATACTGATGACCCATTTCTTTAGCGTCCTTATAGCC
 CGGGGGTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAATATCGG
 ^ ^
 4806 PFLM1, 4807 DRA3,
 ArgAspGlnLeuGluGlnAlaLeuAspCysGluIleTyrGlyAlaCysTyrSerIleGlu
 4862 AGGGACGAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCCTGCTACTCCATAGAA
 TCCCTGGTTCGAACTTGTCCGGGAGCTAACGCTCTAGATGCCCCGACGATGAGGTATCTT
 ^
 4893 BGL2,
 ProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSerLeuHis
 4922 CCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTTCACTCCAC
 GGTGACCTAGATGGAGGTTAGTAAGTTTCTGAGGTACCGGAGTCGCGTAAAAGTGAGGTG
 ^
 4954 NCOI,
 SerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGlyValPro
 4982 AGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGCATGCCTCAGAAAACCTGGGGTACCG
 TCAATGAGAGGTCCACTTTAGTTATCCCACGGCGGTACGGAGTCTTTTGAACCCATGGC
 ^
 5015 SPHI, 5035 KPNI,
 ProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAlaArgGly

FIGURE 14 - Page 9

5042 CCCTTGCGAGCTTGGAGACACCGGGCCCGGAGCGTCCGCGCTAGGCTTCTGGCCAGAGGA
 GGGAACGCTCGAACCTCTGTGGCCCGGGCTCGCAGGCGCGATCCGAAGACCGGTCTCCT
 ^ ^
 5064 APAI, 5091 BALI,
 GlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLysLeuLys
 5102 GGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAAGCTCAAA
 CCGTCCCGACGGTATACACCGTTCATGGAGAAGTTGACCCGTCATTCTTGTTCGAGTTT
 ^ ^ ^ ^
 5113 NDEI,
 LeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAlaGlyTyr
 5162 CTCACTCCAATAGCGGGCCGCTGGCCAGCTGGACTTGTCCGGCTGGTTACGGCTGGCTAC
 GAGTGAGGTTATCGCCGGCGACCGGTCGACCTGAACAGGCCGACCAAGTGCCGACCGATG
 ^ ^ ^ ^
 5174 NOTI, 5175 EAGI XMA3, 5182 BALI, 5186 PVU2,
 SerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrpPheCys
 5222 AGCGGGGGAGACATTTATCACAGCGTGTCTCATGCCCGGCCCCGCTGGATCTGGTTTTGC
 TCGCCCCCTCTGTAAATAGTGTGCGACAGAGTACGGGCGGGGCGACCTAGACCAAAACG
 ^
 5240 DRA3,
 LeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgOP
 5282 CTACTCCTGCTTGCTGCAGGGGTAGGCATCTACCTCCTCCCAACCGATGAATAGTCGAC
 GATGAGGACGAACGACGTCCCCATCCGTAGATGGAGGAGGGGTTGGCTACTTATCAGCTG
 ^ ^
 5295 PSTI, 5336 SALI,

FIGURE 15



FIGURE 16 - Page 1

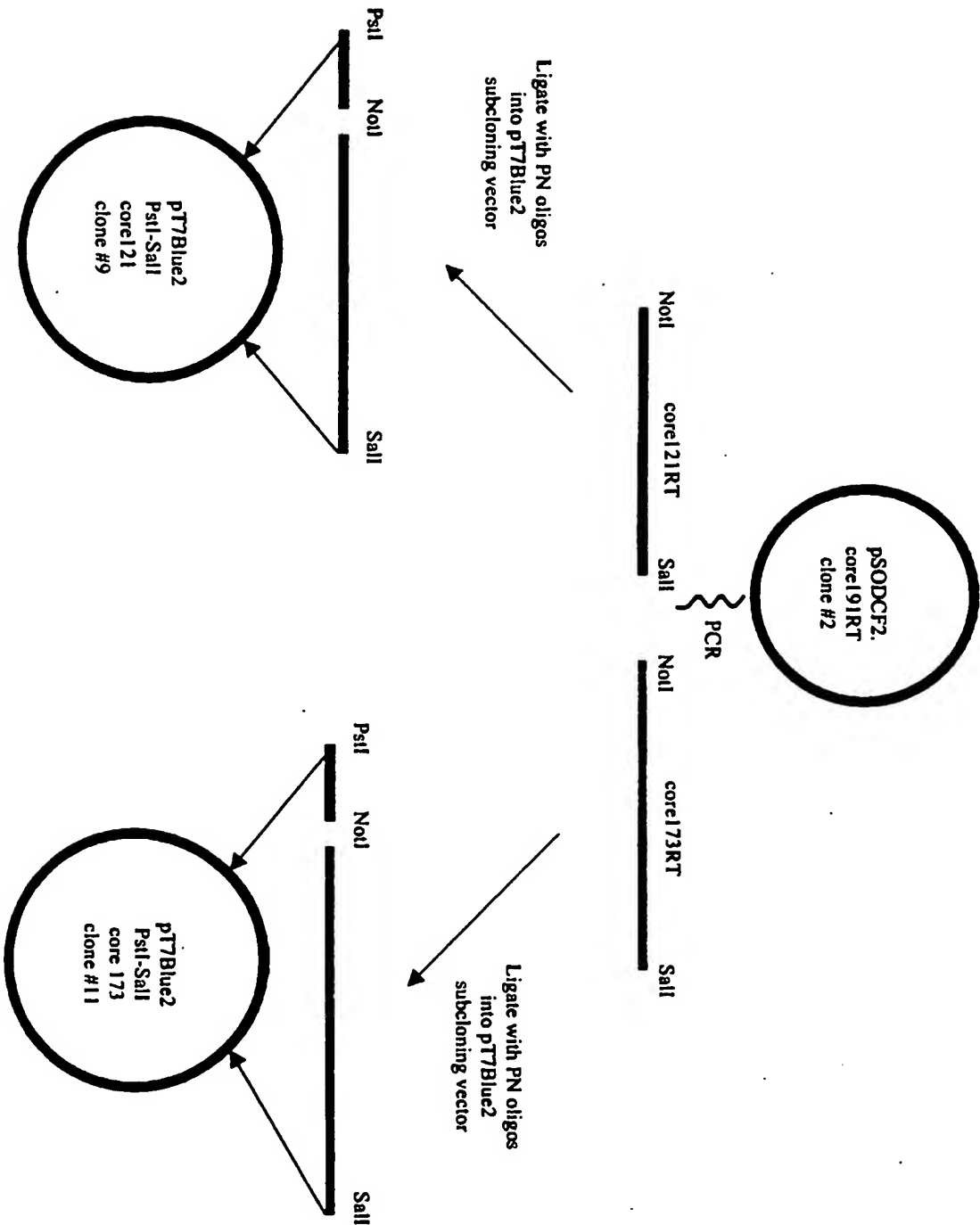


FIGURE 16 - Part 2

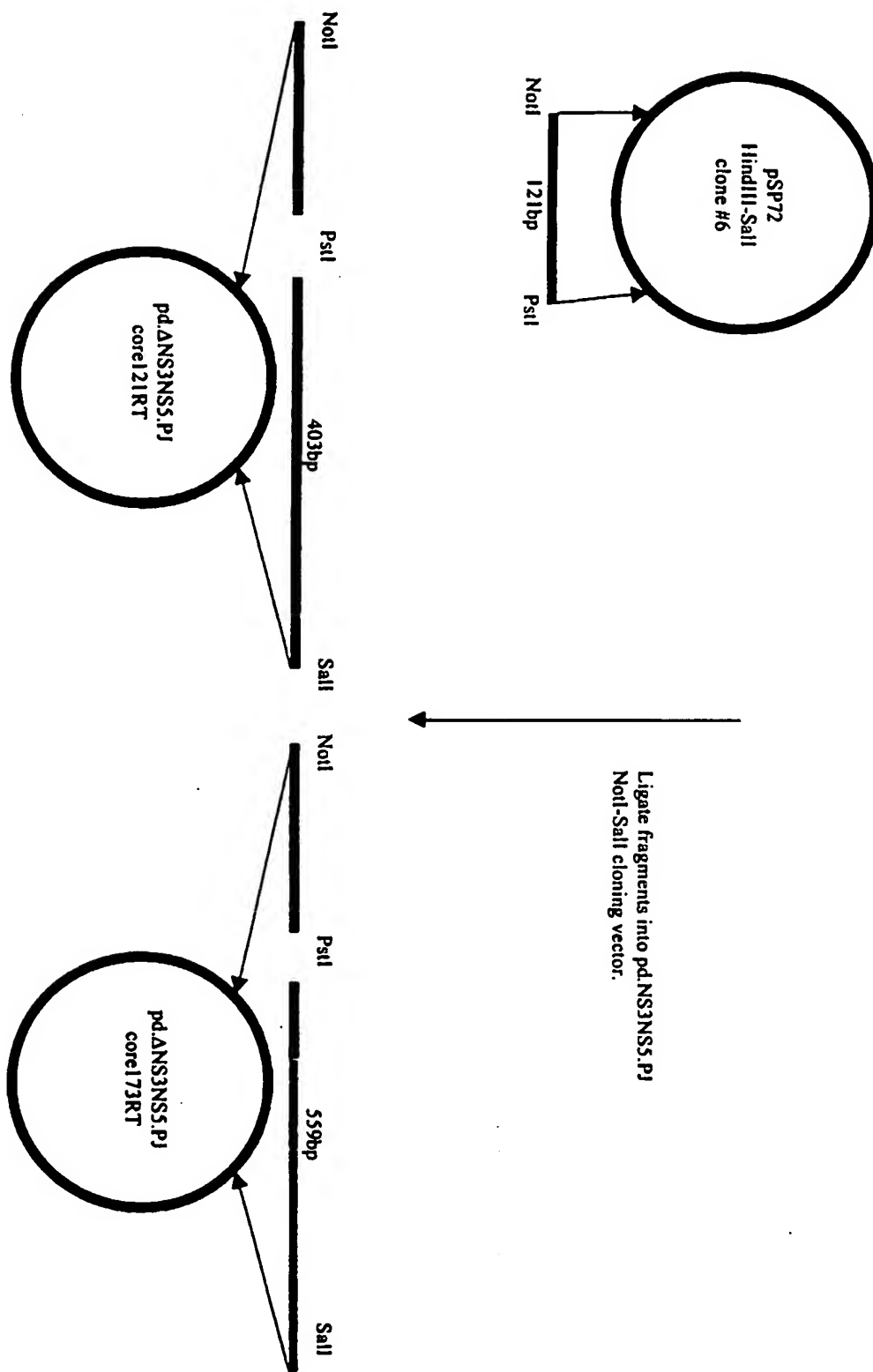


FIGURE 17 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuValLeuAsn
 2 AGCTTACAAAACAAAATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTACTCAAC
 TCGAATGTTTTGTTTTACCGACGTATACGTCGAGTCCCGATATTCCACGATCATGAGTTG
 ^ ^ ^
 1 HIND3, 24 NDEI, 52 SCAI,

ProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGlyIleAsp
 62 CCCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGGATCGAT
 GGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCTTAGCTA
 ^
 116 CLAI,

ProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyrSerThr
 122 CCTAACATCAGGACCGGGTGAGAACAATTACCACTGGCAGCCCCATCACGTACTCCACC
 GGATTGTAGTCCTGGCCCCACTCTTGTTAATGGTGACCGTCGGGGTAGTGTCATGAGGTGG

TyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIleIleCys
 182 TACGGCAAGTTCCTTGCCGACGGCGGGTGCTCGGGGGGCGCTTATGACATAATAATTTGT
 ATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGCAATACTGTATTATTAAACA

AspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeuAspGln
 242 GACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGTCCTTGACCAA
 CTGCTCACGGTGAGGTGCCTACGGTGTAGGTAGAACCGTAACCGTGACAGGAAGTGGTT

AlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGlySerVal
 302 GCAGAGACTGCGGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGCTCCGTC
 CGTCTCTGACGCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGGAGGCCCCGAGGCAG
 ^
 303 ALWN1,

ThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIleProPhe
 362 ACTGTGCCCCATCCCAACATCGAGGAGGTTGCTCTGTCCACCACCGGAGAGATCCCTTTT
 TGACACGGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAGGGAAAA

TyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePheCysHis
 422 TACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTCTGTTCAT
 ATGCCGTTCCGATAGGGGGAGCTTCATTAGTTCCCCCCTCTGTAGAGTAGAAGACAGTA

FIGURE 17 - Page 2

SerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsnAlaVal
 482 TCAAAGAAGAAGTGCACGAACTCGCCGCAAAGCTGGTCGCATTGGGCATCAATGCCGTG
 AGTTTCTTCTTCACGCTGCTTGAGCGGCGTTTCGACCAGCGTAACCCGTAGTTACGGCAC

AlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValValValVal
 542 GCCTACTACCGCGGTCTTGACGTGTCCGTATCCCGACCAGCGGCGATGTTGTCGTCTGTG
 CGGATGATGGGCCAGAACTGCACAGGCAGTAGGGCTGGTCGCCGCTACAACAGCAGCAC

550 SAC2, 560 DRD1,

AlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAspCysAsn
 602 GCAACCGATGCCCTCATGACCGGCTATACCGGCGACTTCGACTCGGTGATAGACTGCAAT
 CGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTGACGTTA

615 BSPH1,

ThrCysValThrGlnThrValAspPheSerLeuAspProThrPheThrIleGluThrIle
 662 ACGTGTGTACCCAGACAGTCGATTTTCAGCCTTGACCCTACCTTCACCATTGAGACAATC
 TGCACACAGTGGGTCTGTCTAGCTAAAGTCGGAACCTGGGATGGAAGTGGTAACCTCTGTTAG

ThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArgGlyLys
 722 ACGTCCCCCAAGATGCTGTCTCCCGCACTCAACGTGGGGCAGGACTGGCAGGGGGAAG
 TCGAGGGGGTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCTGACCGTCCCCCTTC

ProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAspSerSer
 782 CCAGGCATCTACAGATTTGTGGCACCGGGGAGCGCCCTCCGGCATGTTGCACTCGTCC
 GGTCCGTAGATGTCTAAACACCGTGGCCCCCTCGCGGGGAGGCCGTACAAGCTGAGCAGG

816 BGLI, 833 DRD1,

ValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAlaGluThr
 842 GTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTCAGCCCCGCCGAGACT
 CAGGAGACACTCAGATACTGCGTCCGACACGAACCATACTCGAGTGCGGGCGGGCTCTGA

881 SACI,

ThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAspHisLeu
 902 ACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGACCATCTT
 TGTCAATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCCTGGTAGAA

931 SMAI XMAI,

GluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeuSerGln
 962 GAATTTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTATCCCAG
 CTTAAAACCTCCCGCAGAAATGTCCGGAGTGAGTATATCTACGGGTGAAAGATAGGGTC

985 STUI,

ThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrValCysAla
 1022 ACAAGCAGAGTGGGGAGAACCTTCCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCT
 TGTTTCGTCTACCCCTCTTGAAGGAATGGACCATCGCATGGTTCCGGTGGCACACGCGA

1069 DRA3,

ArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArgLeuLys
 1082 AGGGCTCAAGCCCTCCCCCATCGTGGGACCAGATGTGGAAGTGTTTGATTGCCTCAAG

FIGURE 17 - Page 3

TCCCAGATTCTGGGGAGGGGGTAGCACCTGGTCTACACCTTCACAACTAAGCGGAGTTC

ProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsnGluIle
 1142 CCCACCCTCCATGGGCCAACACCCTGCTATACAGACTGGGCGCTGTTTCTCAGAATGAAATC
 GGGTGGGAGGTACCCGGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTACTTTAG
 1150 NCOI,

ThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeuGluVal
 1202 ACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTGGAGGTC
 TGGGACTGCGTGGGTGAGTGGTTTATGTAGTACTGTACGTACAGCCGGCTGGACCTCCAG
 1230 BSPH1, 1234 DRD1, 1237 AVA3, 1245 EAG1 XMA3, 1250 DRD1,

ValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyrCysLeu
 1262 GTCACGAGCACCTGGGTGCTCGTTGGCGGCGTCTGGCTGCTTTGGCCGCGTATTGCTG
 CAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATAACGGAC

SerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAlaIleIle
 1322 TCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCGGGAAGCCGGCAATCATA
 AGTTGTCCGACGCACCACTATCACCCGTCCCAGCAGAACAGGCCCTTCGGCCGTTAGTAT
 1369 NAEI,

ProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGlnHisLeu
 1382 CCTGACAGGGAAGTCTCTACCGAGAGTTCGATGAGATGGAAGAGTGCTCTCAGCACTTA
 GGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCACGAGAGTCGTGAAT
 1385 DRD1,

ProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeuGlyLeu
 1442 CCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAAGCAGAAGGCCCTCGGCCTC
 GGCATGTAGCTCGTTCCCTACTACGAGCGGCTCGTCAAGTTCGTCTCCGGGAGCCGGAG

LeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsnTrpGln
 1502 CTGCAGACCGCGTCCCGTCAGGCAGAGGTTATCGCCCTGCTGTCCAGACCAACTGGCAA
 GACGTCTGGCGCAGGGCAGTCCGTCTCCAATAGCGGGGACGACAGGTCTGGTTGACCGTT
 1502 PSTI, 1507 TTH3I,

LysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGlnTyrLeu
 1562 AAACCTCGAGACCTTCTGGGCGAAGCATATGTGGAACCTTCATCAGTGGGATACAATACTTG
 TTTGAGCTCTGGAAGACCCGCTTCGTATACACCTTGAAGTAGTCACCCTATGTTATGAAC
 1565 XHOI, 1586 NDEI,

AlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPheThrAla
 1622 GCGGGCTTGTCACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTTACAGCT
 CGCCCGAACAGTTGCGACGGACATTGGGGCGGTAACGAAGTAACACCGAAATGTGCA
 1643 BSTE2, 1677 ALWN1 PVU2,

AlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGlyGlyTrp
 1682 GCTGTCAACAGCCCACTAACCCTAGCCAAACCTCCTCTTCAACATATTGGGGGGGTGG
 CGACAGTGGTGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCCCCCACC

FIGURE 17 - Page 4

ValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGlyLeuAla
 1742 GTGGCTGCCAGCTCGCCGCCCGGTGCCGCTACTGCCTTTGTGGCGCTGGCTTAGCT
 CACCGACGGGTCGAGCGGGGGGCCACGGCGATGACGGAAACACCCGCGACCGAATCGA
 1794 ESP1,
 GlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAlaGlyTyr
 1802 GGCGCCGCCATCGGCAGTGTGGACTGGGGAAGGTCCTCATAGACATCCTTGCAGGGTAT
 CCGCGGCGGTAGCCGTACAACTGACCCCTTCCAGGAGTATCTGTAGGAACGTCCCATTA
 1802 KAS1 NARI,
 GlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluValProSer
 1862 GGCGCGGGCGTGGCGGGAGCTCTTGTGGCATTCAAGATCATGAGCGGTGAGGTCCCTCC
 CCGCGCCCGCACCGCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAGGGGAGG
 1878 SAC1, 1899 BSPH1,
 ThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuValValGly
 1922 ACGGAGGACCTGGTCAATCTACTGCCCGCCATCCTCTCGCCCGGAGCCCTCGTAGTCGGC
 TGCCCTCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGGCCTCGGGAGCATCAGCCG
 1928 TTH3I,
 ValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaValGlnTrp
 1982 GTGGTCTGTGCAGCAATACTGCGCCGGCACGTTGGCCCGGGCGAGGGGGCAGTGCAGTGG
 CACCAGACACGTCGTTATGACGGCGCCGTGCAACCGGGCCCGCTCCCCCGTCACGTCACC
 2004 NAEI, 2017 SMAI XMAI,
 MetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal
 2042 ATGAACCGGCTGATAGCCTTCGCCTCCCGGGGAACCATGTTTCCCCACGCACTACGTG
 TACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGTGCGTGATGCAC
 2067 SMAI XMAI, 2093 DRA3,
 ProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrValThrGln
 2102 CCGGAGAGCGATGCAGCTGCCCGCGTCACTGCCATACTCAGCAGCCTCACTGTAACCCAG
 GGCTCTCGCTACGTCGACGGGCGCAGTGACGGTATGAGTCGTCGGAGTGACATTGGGTC
 2115 PVU2, 2159 ALWN1,
 LeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSerGlySer
 2162 CTCCTGAGGCGACTGCACCACTGGATAAGCTCGGAGTGTAACCTCCATGCTCCGTTCC
 GAGGACTCCGCTGACGTGGTCACCTATTTCGAGCCTCACATGGTGAGGTACGAGGCCAAGG
 2164 MST2, 2220 ECON1,
 TrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThrTrpLeu
 2222 TGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACCTGGCTA
 ACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGGACCGAT
 LysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArgGlyTyr
 2282 AAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCTTTGTGTCTGCCAGCGCGGGTAT
 TTTCGATTGAGTACGGTGTGACGGACCCTAGGGGAAACACAGGACGGTTCGCGCCCATTA
 2285 ESP1, 2300 PVU2, 2310 BAMHI,

FIGURE 17 - Page 5

LysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAlaGluIle
 2342 AAGGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGCTGCCACTGTGGAGCTGAGATC
 TTCCCCAGACCGCTCCCCTGCCGTAGTACGTGTGAGCGACGGTGACACCTCGACTCTAG
 ThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArgAsnMet
 2402 ACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCCTAGGACCTGCAGGAACATG
 TGACCTGTACAGTTTTTGGCCTGCTACTCCTAGCAGCCAGGATCCTGGACGTCTTGTAC
 ^ ^ ^
 2425 BSAB1, 2441 AVR2, 2448 SSE83871, 2449 PSTI,
 TrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeuProAla
 2462 TGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGCCCTGTACCCCCCTTCTCGCG
 ACCTCACCTGGAAGGGGTAATTACGGATGTGGTGCCCGGGACATGGGGGGAAGGACGC
 ^ ^
 2480 ASE1, 2497 APAI,
 ProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIleArgGln
 2522 CCGAACTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATAAGGCAG
 GGCTTGATGTGCAAGCGGATACCTCCCACAGACGTCTCCTTATGCACCTCTATTCCGTC
 ^
 2553 PSTI,
 ValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysProCysGln
 2582 GTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCGTGCCAG
 CACCCCTGAAGGTGATGCACTGCCCATACTGATGACTGTTAGAATTTACGGGCACGGTC
 ^
 2594 DRA3,
 ValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPheAlaPro
 2642 GTCCCATCGCCGAATTTTTACAGAATTGGACGGGGTGCGCCTACATAGGTTTGCGCCC
 CAGGGTAGCGGGCTTAAAAAGTGTCTTAACCTGCCCCACGCGGATGTATCAAACGCGGG
 ProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGluTyrPro
 2702 CCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTCAGAGTAGGACTCCACGAATACCCG
 GGGACGTTGCGGAACGACGCCCTCCTCCATAGTAAGTCTCATCTGAGGTGCTTATGGGC
 ^
 2757 HGIE2,
 ValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSerMetLeu
 2762 GTAGGGTCGCAATTACCTTGCGAGCCCGAACCGGACGTGGCCGTGTGACGTCCATGCTC
 CATCCACGCTTAATGGAACGCTCGGGCTTGGCCTGCACCGGCACAACCTGCAGGTACGAG
 ^
 2809 AAT2,
 ThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGlySerPro
 2822 ACTGATCCCTCCCATATAACAGCAGAGGCGGCCGGCGAAGGTTGGCGAGGGGATCACCC
 TGACTAGGGAGGGTATATTGTCGTCTCCGCCGGCCCGCTTCCAACCGCTCCCTAGTGGG
 ^
 2850 EAG1 XMA3,
 ProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAlaThrCys
 2882 CCCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCAACTTGC
 GGGAGACACCGGTCGAGGAGCCGATCGGTGATAGGCGAGGTAGAGAGTTCGGTTGAACG
 ^ ^
 2889 BALI, 2903 NHEI,

FIGURE 17 - Page 6

ThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrpArgGln
 2942 ACCGCTAACCATGACTCCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGGAGGCAG
 TGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGGTTGGAGGATACCTCCGTC
 2966 ESP1, 2969 SAC1,
 GluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeuAspSer
 3002 GAGATGGGCGGCAACATCACCAGGGTTGAGTCAGAAAACAAAGTGGTGATTCTGGACTCC
 CTCTACCCGCCGTTGTAGTGGTCCCAACTCAGTCTTTTGTTCACCACTAAGACCTGAGG
 PheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGluIleLeu
 3062 TTCGATCCGCTTGTGGCGGAGGAGGACGAGCGGGAGATCTCCGTACCCGCAGAAATCCTG
 AAGCTAGGCGAACACCGCCTCCTCTGCTCGCCCTCTAGAGGCATGGGCGTCTTTAGGAC
 3096 BGL2,
 ArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyrAsnPro
 3122 CGGAAGTCTCGGAGATTCGCCCAGGCCCTGCCCGTTTGGGCGCGGCCGGACTATAACCCC
 GCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGGCCTGATATTGGGG
 3143 ALWN1, 3164 EAG1 XMA3,
 ProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGlyCysPro
 3182 CCGCTAGTGGAGACGTGGAAAAGCCCGACTACGAACACCTGTGGTCCATGGCTGCCCG
 GCGGATCACCTCTGCACCTTTTTCGGGCTGATGCTTGGTGGACACCAGGTACCGACGGG
 3217 HGIE2, 3229 NCOI,
 LeuProProProLysSerProProValProProProArgLysLysArgThrValValLeu
 3242 CTTCACCTCCAAAGTCCCCTCCTGTGCCTCCGCCTCGGAAGAAGCGGACGGTGGTCTC
 GAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTTCGCCTGCCACCAGGAG
 ThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGlySerSer
 3302 ACTGAATCAACCCTATCTACTGCCTTGGCCGAGCTCGCCACCAGAAAGCTTTGGCAGCTCC
 TGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCGTCGAGG
 3332 SACI, 3346 HIND3,
 SerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaProSerGly
 3362 TCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCCTTCTGGC
 AGTTGAAGGCCGTAATGCCCCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGAAGACCG
 CysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGlyGluPro
 3422 TGCCCCCCCCGACTCCGACGCTGAGTCCTATTCTCCATGCCCCCCTGGAGGGGGGAGCCT
 ACGGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCCCTCGGA
 3437 EAM11051,
 GlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsnAlaGlu
 3482 GGGGATCCGGATCTTAGCGACGGGTATGGTCAACGGTCAGTAGTGAGGCCAACGCGGAG
 CCCCTAGGCCTAGAATCGCTGCCAGTACCAGTTGCCAGTCATCACTCCGGTTGCGCCTC
 3484 BAMHI, 3485 BSAB1, 3487 BSPE1,
 AspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrProCysAla
 3542 GATGTCGTGTGCTGCTCAATGTCTTACTCTTGGACAGGCGCACTCGTCACCCCGTGGGCC
 CTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCGCGTGAGCAGTGGGGCACGCGG

FIGURE 17 - Page 7

3589 DRA3, 3600 SAC2, -

AlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHisHisAsn
 3602 GCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTACCCACAAT
 CGCCTTCTTGTCTTTGACGGGTAGTTACGTGATTTCGTTGAGCAACGATGCAGTGGTGTTA

3611 ALWN1, 3655 PFLM1,

LeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThrPheAsp
 3662 TTGGTGTATTCCACCACCTCACGCAGTGCTTGCCAAAGGCAGAAGAAAGTCACATTTGAC
 AACCACATAAGGTGGTGGAGTGCGTCACGAACGGTTTCCGTCTTCTTTTCAGTGTAAGT

3681 DRA3,

ArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAlaAlaAla
 3722 AGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCAGCGGCG
 TCTGACGTTCAAGACCTGTCGGTAATGGTCCTGCATGAGTTCCTCCAATTTTCGTCGCGCG

SerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrProProHis
 3782 TCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGACGCTGACGCCCCACAC
 AGTTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTCGGACTGCGGGGGTGTG

3816 HIND3,

SerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArgLysAla
 3842 TCAGCCAAATCCAAGTTTGTTATGGGGCAAAGACGTCCGTTGCCATGCCAGAAAGGCC
 AGTCGGTTTAGGTTCAAACCAATACCCGTTTTCTGCAGGCAACGGTACGGTCTTCCGG

3875 AAT2, 3890 BGLI,

ValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrProIleAsp
 3902 GTAACCCACATCAACTCCGTGTGGAAGACCTTCTGGAAGACAATGTAACCAATAGAC
 CATTGGGTGTAGTTGAGGCACACCTTTCTGGAAGACCTTCTGTTACATTGTGGTTATCTG

ThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGlyArgLys
 3962 ACTACCATCATGGCTAAGAACGAGGTTTTCTGCGTTTCAGCCTGAGAAGGGGGTTCGTAAG
 TGATGGTAGTACCGATTCTTGCTCCAAAAGACGCAAGTCGGACTCTTCCCCCAGCATT

ProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMetAlaLeu
 4022 CCAGCTCGTCTCATCGTGTCCCCGATCTGGGCGTGCAGCGTGTGCGAAAAGATGGCTTTG
 GGTGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACACGCTTTTCTACCGAAAC

TyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPheGlnTyr
 4082 TACGACGTGGTTACAAAGCTCCCTTGCCGTGATGGGAAGCTCCTACGGATTCCAATAC
 ATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCCTTCGAGGATGCCTAAGGTTATG

SerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThrProMet
 4142 TCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGGAAGTCCAAGAAAACCCAATG
 AGTGGTCTGTCGCCCCAATTAAGGAGCACGTTTCGCACCTTCAGGTTCTTTTGGGGTTAC

4160 ECORI,

GlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIleArgThr
 4202 GGGTTCTCGTATGATACCCGCTGCTTTGACTCCACAGTCACTGAGAGCGACATCCGTACG
 CCCAAGAGCATACTATGGGCGACGAACTGAGGTGTCAGTGACTCTCGCTGTAGGCATGC

FIGURE 17 - Page 8

4229 DRD1, 4236 ALWN1,
 GluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIleLysSer
 4262 GAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCAAGCCCGCGTGGCCATCAAGTCC
 CTCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTCTGGGCGCACCGGTAGTTCAGG
 4301 BGLI, 4308 BALI,
 LeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsnCysGly
 4322 CTCACCGAGAGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAACTGCGGC
 GAGTGGCTCTCCGAAATACAACCCCGGAGAAATGGTTAAGTCCCCCTCTTGACGCCG
 4345 APAI,
 TyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeuThrCys
 4382 TATCGCAGGTGCCGCGCGAGCGGCGTACTGACAACCTAGCTGTGGTAACACCCTCACTTGC
 ATAGCGTCCACGGCGCGCTCGCCGCATGACTGTTGATCGACACCATTTGTGGGAGTGAACG
 TyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMetLeuVal
 4442 TACATCAAGGCCCGGGCAGCCTGTCGAGCCGAGGGCTCCAGGACTGCACCATGCTCGTG
 ATGTAGTTCCGGGCCCGTCCGACAGCTCGGCGTCCCGAGGTCCTGACGTGGTACGAGCAC
 4452 SMAI XMAI,
 CysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAlaAlaSer
 4502 TGTGGCGACGACTTAGTCGTTATCTGTGAAAGCGCGGGGTCCAGGAGGACGCGCGGAGC
 ACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCTCTCGCGCGCTCG
 4508 DRD1, 4511 TTH3I,
 LeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspProProGln
 4562 CTGAGAGCCTTACGGAGGCTATGACCAGGTACTCCGCCCCCTGGGGACCCCCACAA
 GACTCTCGGAAGTGCCTCCGATACTGGTCCATGAGGCGGGGGGACCCCTGGGGGTGTT
 ProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAlaHisAsp
 4622 CCAGAATACGACTTGGAGCTCATAACATCATGCTCCTCCAACGTGTCAGTCGCCCACGAC
 GGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGGGTGCTG
 4637 SACI,
 GlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAlaArgAla
 4682 GGCGCTGGAAAGAGGGTCTACTACCTCACCCGTGACCCTACAACCCCTCGCGAGAGCT
 CCGCGACCTTTCTCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGGAGCGCTCTCGA
 4731 NRUI,
 AlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIleMetPhe
 4742 GCGTGGGAGACAGCAAGACACACTCCAGTCAATTCCTGGCTAGGCAACATAATCATGTTT
 CGCACCTCTGTCGTTCTGTGTGAGGTGAGTTAAGGACCGATCCGTTGTATTAGTACAAA
 AlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeuIleAla
 4802 GCGGGGCTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAATATCGG
 4806 PFLM1, 4807 DRA3,
 ArgAspGlnLeuGluGlnAlaLeuAspCysGluIleTyrGlyAlaCysTyrSerIleGlu

FIGURE 17 - Page 9

4862 AGGGACCAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCCTGCTACTCCATAGAA
 TCCCTGGTCCGAACCTGTCCGGGAGCTAACGCTCTAGATGCCCCGGACGATGAGGTATCTT
 4893 BGL2,

ProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSerLeuHis
 4922 CCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTCCTACTCCAC
 GGTGACCTAGATGGAGGTTAGTAAGTTCTGAGGTACCGGAGTCGCGTAAAAGTGAGGTG
 4954 NCOI,

SerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGlyValPro
 4982 AGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGCATGCCTCAGAAAACCTGGGGTACCG
 TCAATGAGAGGTCCACTTTAGTTATCCACCGGCGTACGGAGTCTTTGAACCCCATGGC
 5015 SPHI, 5035 KPN1,

ProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAlaArgGly
 5042 CCCTTGCGAGCTTGGAGACACCGGGCCCGAGCGTCCGCGCTAGGCTTCTGGCCAGAGGA
 GGGAACGCTCGAACCTCTGTGGCCCGGGCCTCGCAGGCGCGATCCGAAGACCGGTCTCCT
 5064 APAI, 5091 BALI,

GlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLysLeuLys
 5102 GGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAAGCTCAA
 CCGTCCCGACGGTATACACCGTTCATGGAGAAGTTGACCCGTCATTCTTGTTCGAGTTT
 5113 NDEI,

LeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAlaGlyTyr
 5162 CTCCTCCAATAGCGCCGCTGGCCAGCTGGACTTGTCCGGCTGGTTACCGGCTGGCTAC
 GAGTGAGGTTATCGCCGGCGACCGGTGACCTGAACAGGCCGACCAAGTGCCGACCGATG
 5174 NOTI, 5175 EAGI XMA3, 5182 BALI, 5186 PVU2,

SerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrpPheCys
 5222 AGCGGGGGAGACATTTATCACAGCGTGTCTCATGCCCGGCCCGCTGGATCTGGTTTTGC
 TCGCCCCCTCTGTAAATAGTGTGCGACAGAGTACGGGCCGGGGCGACCTAGACCAAAACG
 5240 DRA3,

LeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgMetSerThrAsn
 5282 CTACTCCTGCTTGCTGCAGGGGTAGGCATCTACCTCCTCCCAACCGAATGAGCACGAAT
 GATGAGGACGAACGACGTCCCCATCCGTAGATGGAGGAGGGGTGGCTTACTCGTGCTTA
 5295 PSTI,

ProLysProGlnArgLysThrLysArgAsnThrAsnArgArgProGlnAspValLysPhe
 5342 CCTAAACCTCAAAGAAAGACCAAACGTAACACCAACCGCGGCCGCGAGGACGTCAAGTTC
 GGATTTGGAGTTTCTTTCTGGTTTGCAATTGTGGTTGGCCGCCGGCGTCTGCAGTTCAAG
 5380 NOTI, 5381 EAGI XMA3, 5390 AAT2, 5401 SMAI XMAI,

ProGlyGlyGlyGlnIleValGlyGlyValTyrLeuLeuProArgArgGlyProArgLeu
 5402 CCGGGTGGCGGTGATCGTTGGTGGAGTTTACTTGTGCGCGCAGGGGCCCTAGATTG
 GGCCACCGCCAGTCTAGCAACCACCTCAAATGAACAACGGCGCGTCCCCGGGATCTAAC

FIGURE 17 - Page 10

5449 APAI,

GlyValArgAlaThrArgLysThrSerGluArgSerGlnProArgGlyArgArgGlnPro
 5462 GGTGTGCGCGCGACGAGAAAGACTTCCGAGCGGTCGCAACCTCGAGGTAGACGTCAGCCT
 CCACACGCGCGCTGCTCTTTCTGAAGGCTCGCCAGCGTTGGAGCTCCATCTGCAGTCGGA
 ^ ^ ^ ^ ^

5467 BSSH2, 5478 XMNI, 5502 XHOI, 5511 AAT2,

IleProLysAlaArgArgProGluGlyArgThrTrpAlaGlnProGlyTyrProTrpPro
 5522 ATCCCCAAGGCTCGTCGGCCCGAGGGCAGGACCTGGGCTCAGCCCGGGTACCCTTGGCCC
 TAGGGGTTCCGAGCAGCCGGGCTCCCGTCCTGGACCCGAGTCGGGCCCATGGGAACC3GG
 ^ ^ ^ ^ ^

5548 ALWN1, 5558 ESP1, 5564 SMAI XMAI, 5568 KPNI,

LeuTyrGlyAsnGluGlyCysGlyTrpAlaGlyTrpLeuLeuSerProArgGlySerArg
 5582 CTCTATGGCAATGAGGGCTGCGGGTGGGCGGGATGGCTCCTGTCTCCCCGTGGCTCTCGG
 GAGATACCGTTACTCCCGACGCCACCCGCCCTACCGAGGACAGAGGGGCACCGAGAGCC

ProSerTrpGlyProThrAspProArgArgArgSerArgAsnLeuGlyLysOC AM
 5642 CCTAGCTGGGGCCCCACAGACCCCGCGTAGGTCGCGCAATTGGGTAAGTAATAGTCG
 GGATCGACCCCGGGGTGTCTGGGGCCGCATCCAGCGCGTTAAACCCATTATTATCAGC
 ^ ^ ^ ^ ^

5650 APAI, 5698 SALI,

5702 AC
 TG

FIGURE 18 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuValLeuAsn
 2 AGCTTACAAAACAAAATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTACTCAAC
 TCGAATGTTTTGTTTTACCGACGTATACGTCGAGTCCCGATATTCCACGATCATGAGTTG
 ^ ^ ^
 1 HIND3, 24 NDEI, 52 SCAI,

ProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGlyIleAsp
 62 CCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGGATCGAT
 GGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCCCTAGCTA
 ^
 116 CLAI,

ProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyrSerThr
 122 CCTAACATCAGGACCGGGGTGAGAACAATTACCACTGGCAGCCCCATCACGTACTCCACC
 GGATTGTAGTCTCGCCCCACTCTTGTTAATGGTGACCGTCGGGGTAGTGCATGAGGTGG

TyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIleIleCys
 182 TACGGCAAGTTCCTTGCCGACGGCGGGTGCTCGGGGGGCGCTTATGACATAATAATTTGT
 ATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGGAATACTGTATTATTAAACA

AspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeuAspGln
 242 GACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGTCTTGACCAA
 CTGCTCACGGTGAGGTGCTACGGTGTAGGTAGAACCCGTAACCGTGACAGGAAGTGGTT

AlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGlySerVal
 302 GCAGAGACTGCGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGCTCCGTC
 CGTCTCTGACGCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGGAGGCCGAGGCAG
 ^
 303 ALWN1,

ThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIleProPhe
 362 ACTGTGCCCCATCCCAACATCGAGGAGTTGCTCTGTCCACCACCGGAGAGATCCCTTTT
 TGACACGGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAGGGAAAA

TyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePheCysHis
 422 TACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTCTGTCTAT
 ATGCCGTTCCGATAGGGGGAGCTTCATTAGTTCCTCCCCCTCTGTAGAGTAGAAGACAGTA

SerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsnAlaVal
 482 TCAAAGAAGAAGTGCGACGAACCTCGCCGCAAAGCTGGTTCGCATTGGGCATCAATGCCGTG
 AGTTTCTTCTTCACGCTGCTTGAGCGGCGTTTCGACCAGCGTAACCCGTAGTTACGGCAC

AlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValValValVal
 542 GCCTACTACCGCGGTCTTGACGTGTCCGTATCCCGACCGCGGATGTTGTGTCGTG
 CGGATGATGGCGCCAGAACTGCACAGGCAGTAGGGCTGGTTCGCGCTACAACAGCAGCAC
 ^ ^ ^
 550 SAC2, 560 DRD1,

AlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAspCysAsn
 602 GCAACCGATGCCCTCATGACCGGCTATACCGGCGACTTCGACTCGGTGATAGACTGCAAT
 CGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTGACGTTA
 ^

FIGURE 18 - Page 2

ThrCysValThrGlnThrValAspPheSerLeuAspProThrPheThrIleGluThrIle
 662 ACGTGTGTACCCAGACAGTCGATTTTCAGCCTTGACCCTACCTTCACCATTGAGACAATC
 TGCACACAGTGGGTCTGTCTAGCTAAAGTCGGAAGTGGGATGGAAGTGGTAACTCTGTTAG

ThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArgGlyLys
 722 ACCTCCCCAAGATGCTGTCTCCCGCACTCAACGTCGGGGCAGGACTGGCAGGGGGAAG
 TCGAGGGGGTTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCCTGACCGTCCCCCTTC

ProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAspSerSer
 782 CCAGGCATCTACAGATTTGTGGCACCAGGGGAGCGCCCTCCGGCATGTTCCGACTCGTCC
 GGTCCGTAGATGTCTAAACACCGTGGCCCCCTCGCGGGGAGGCCGTACAAGCTGAGCAGG

816 BGLI, 833 DRD1,

ValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAlaGluThr
 842 GTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTCACGCCCCGCGAGACT
 CAGGAGACACTCACGATACTGCGTCCGACACGAACCATACTCGAGTGCGGGCGGCTCTGA

881 SACI,

ThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAspHisLeu
 902 ACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGACCATCTT
 TGTCATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCCTGGTAGAA

931 SMAI XMAI,

GluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeuSerGln
 962 GAATTTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTATCCAG
 CTTAAAACCTCCCGCAGAAATGTCCGGAGTGAGTATATCTACGGGTGAAAGTAGGGTC

985 STUI,

ThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrValCysAla
 1022 ACAAGCAGAGTGGGGAGAACCCTTCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCT
 TGTTTCGTCTACCCCTCTTGAAGGAATGGACCATCGCATGGTTCGGTGGCACACGCGA

1069 DRA3,

ArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArgLeuLys
 1082 AGGGCTCAAGCCCCTCCCCATCGTGGGACCAGATGTGGAAGTGTGTTGATTCGCCTCAAG
 TCCCGAGTTCGGGGAGGGGTAGCACCCCTGGTCTACACCTTCACAACTAAGCGGAGTTC

ProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsnGluIle
 1142 CCCACCCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTCAGAATGAAATC
 GGGTGGGAGGTACCCGGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTACTTTAG

1150 NCOI,

ThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeuGluVal
 1202 ACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTGGAGGTC
 TGGGACTGCGTGGGTCACTGGTTTATGTAGTACTGTACGTACAGCCGGCTGGACCTCCAG

1230 BSPH1, 1234 DRD1, 1237 AVA3, 1245 EAG1 XMA3, 1250 DRD1,

ValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyrCysLeu
 1262 GTCACGAGCACCTGGGTGCTCGTTGGCGGCGTCCTGGCTGCTTTGGCCGCGTATTGCCTG

FIGURE 18 - Page 3

CAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATAACGGAC
 SerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAlaIleIle
 1322 TCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCGGGAAGCCGGCAATCATA
 AGTTGTCCGACGCACCACTATCACCCGTCCCAGCAGAACAGGCCCTTCGGCCGTTAGTAT
 1369 NAEI,
 ProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGlnHisLeu
 1382 CCTGACAGGGAAGTCCTCTACCGAGAGTTCGATGAGATGGAAGAGTGCTCTCAGCACTTA
 GGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCAGAGAGTCGTGAAT
 1385 DRD1,
 ProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeuGlyLeu
 1442 CCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAAGCAGAAGGCCCTCGGCCTC
 GGCATGTAGCTCGTTCCTACTACGAGCGGCTCGTCAAGTTCGTCTTCGGGAGCCGGAG
 LeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsnTrpGln
 1502 CTGCAGACCGCGTCCCGTCAGGCAGAGTTATCGCCCCGTGTGTCAGACCAACTGGCAA
 GACGTCTGGCGCAGGGCAGTCCGTCTCAATAGCGGGGACGACAGGTCTGGTTGACCGTT
 1502 PSTI, 1507 TTH3I,
 LysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGlnTyrLeu
 1562 AAATCGAGACCTTCTGGGCGAAGCATATGTGGAACCTCATCAGTGGGATACAATACTTG
 TTTGAGCTCTGGAAGACCCGCTTCGTATACCTTGAAGTAGTCACCCTATGTTATGAAC
 1565 XHOI, 1586 NDEI,
 AlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPheThrAla
 1622 GCGGGCTTGTCACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTTACAGCT
 CGCCCGAACAGTTGCGACGACCATTTGGGGCGGTAACGAAGTAACTACCGAAAATGTCGA
 1643 BSTE2, 1677 ALWN1 PVU2,
 AlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGlyGlyTrp
 1682 GCTGTCAACAGCCCACTAACCCTAGCCAAACCCTCCTCTCAACATATTGGGGGGGTGG
 CGACAGTGGTGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCCCCCACC
 ValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGlyLeuAla
 1742 GTGGCTGCCCAGCTCGCCGCCCCCGGTGCCGCTACTGCCTTTGTGGGCGCTGGCTTAGCT
 CACCGACGGGTCGAGCGGCGGGGCCACGGCGATGACGGAAACACCGCGACCGAATCGA
 1794 ESP1,
 GlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAlaGlyTyr
 1802 GCGCGCCCATCGGCAGTGTGGACTGGGGAAGGTCCTCATAGACATCCTGCAGGGTAT
 CCGCGGCGGTAGCCGTCACAACCTGACCCCTTCAGGAGTATCTGTAGGAACGTCCCAT
 1802 KAS1 NARI,
 GlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluValProSer
 1862 GCGCGGGCGGTGGCGGGAGCTCTTGTGGCATTCAAGATCATGAGCGGTGAGGTCCCCTCC
 CCGCGCCCGCACCGCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAGGGGAGG
 1878 SACI, 1899 BSPH1,

FIGURE 18 - Page 4

ThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuValValGly
 1922 ACGGAGGACCTGGTCAATCTACTGCCCGCCATCCTCTCGCCCGGAGCCCTCGTAGTCGGC
 TGCCTCCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGGCCTCGGGAGCATCAGCCG
 ^
 1928 TTH3I,
 ValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaValGlnTrp
 1982 GTGGTCTGTGCAGCAATACTGCGCCGGCAGTTGGCCCGGGCGAGGGGGCAGTGCAGTGG
 CACCAGACACGTCGTTATGACGCGGCCGTGCAACCGGGCCCGCTCCCCGTCACGTACC
 ^ ^
 2004 NAEI, 2017 SMAI XMAI,
 MetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal
 2042 ATGAACCGGCTGATAGCCTTCGCCTCCCGGGGAACCATGTTTCCCCACGCACTACGTG
 TACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGTGCGTGATGCAC
 ^ ^
 2067 SMAI XMAI, 2093 DRA3,
 ProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrValThrGln
 2102 CCGGAGAGCGATGCAGCTGCCCGCGTCACTGCCATACTCAGCAGCCTCACTGTAACCCAG
 GGCCTCTCGCTACGTCGACGGGCGCAGTGACGGTATGAGTCGTCGGAGTGACATTGGGTC
 ^ ^
 2115 PVU2, 2159 ALWN1,
 LeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSerGlySer
 2162 CTCCTGAGGCGACTGCACCAGTGGATAAGCTCGGAGTGTACCACTCCATGCTCCGGTTCC
 GAGGACTCCGCTGACGTGGTCACCTATTCGAGCCTCACATGGTGAGGTACGAGGCCAAGG
 ^ ^
 2164 MST2, 2220 ECON1,
 TrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThrTrpLeu
 2222 TGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACCTGGCTA
 ACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGGACCGAT
 LysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArgGlyTyr
 2282 AAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCCCTTTGTGTCCTGCCAGCGCGGGTAT
 TTTCGATTTCGAGTACGGTGTTCGACGGACCCTAGGGGAAACACAGGACGGTTCGCGCCCAT
 ^ ^ ^
 2285 ESP1, 2300 PVU2, 2310 BAMHI,
 LysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAlaGluIle
 2342 AAGGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGCTGCCACTGTGGAGCTGAGATC
 TTCCCCCAGACCGCTCCCCTGCCGTAGTACGTGTGAGCGACGGTGACACCTCGACTCTAG
 ThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArgAsnMet
 2402 ACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCCTAGGACCTGCAGGAACATG
 TGACCTGTACAGTTTTTGGCCTGCTACTCCTAGCAGCCAGGATCCTGGACGTCCTTGATC
 ^ ^ ^
 2425 BSAB1, 2441 AVR2, 2448 SSE83871, 2449 PSTI,
 TrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeuProAla
 2462 TGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGCCCCCTGTACCCCCCTTCCTGCG
 ACCTCACCTGGAAGGGGTAATTACGGATGTGGTGGCCGGGGACATGGGGGGAAGGACGC
 ^ ^
 2480 ASE1, 2497 APAI,

FIGURE 18 - Page 5

ProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIleArgGln
 2522 CCGAACTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATAAGGCAG
 GGCTTGATGTGCAAGCGCGATACCTCCACAGACGTCTCCTTATGCACCTCTATTCCGTC
 2553 PSTI,
 ValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysProCysGln
 2582 GTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCGTGCCAG
 CACCCCTGAAGGTGATGCACTGCCCATACTGATGACTGTTAGAATTTACGGGCACGGTC
 2594 DRA3,
 ValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPheAlaPro
 2642 GTCCCATCGCCCGAATTTTTCACAGAATTGGACGGGGTGCGCCTACATAGGTTTGCGCCC
 CAGGGTAGCGGGCTTAAAAAGTGTCTTAACCTGCCCCACGCGGATGTATCCAAACGCGGG
 ProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGluTyrPro
 2702 CCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTAGAGTAGGACTCCACGAATACCCG
 GGGACGTTTCGGGAACGACGCCCTCCTCCATAGTAAGTCTCATCTGAGGTGCTTATGGGC
 2757 HGIE2,
 ValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSerMetLeu
 2762 GTAGGGTCGCAATTACCTTGCGAGCCCGAACCGGACGTGGCCGTGTTGACGTCCATGCTC
 CATCCAGCGTTAATGGAACGCTCGGGCTTGGCTGCACCGGCACAACTGCAGGTACGAG
 2809 AAT2,
 ThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGlySerPro
 2822 ACTGATCCCTCCCATATAACAGCAGAGGCGGCCGGGCGAAGGTTGGCGAGGGGATCACCC
 TGAAGTAGGGAGGTTATATTGTCGTCTCCGCCGCGCCGCTTCCAACCGCTCCCTAGTGGG
 2850 EAG1 XMA3,
 ProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAlaThrCys
 2882 CCCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCAACTTGC
 GGGAGACACCGGTCGAGGAGCCGATCGGTCGATAGGCGAGGTAGAGAGTTCCGTTGAACG
 2889 BALI, 2903 NHEI,
 ThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrpArgGln
 2942 ACCGCTAACCATGACTCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGGAGGCAG
 TGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGGTTGGAGGATACCTCCGTC
 2966 ESP1, 2969 SACI,
 GluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeuAspSer
 3002 GAGATGGGCGGCAACATCACCGAGGTTGAGTCAGAAAACAAAGTGGTGATTCTGGACTCC
 CTCTACCCGCCGTTGTAGTGGTCCCAACTCAGTCTTTTGTTCACCACTAAGACCTGAGG
 PheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGluIleLeu
 3062 TTCGATCCGCTTGTGGCGGAGGAGGACGAGCGGGAGATCTCCGTACCCGCAGAAATCCTG
 AAGCTAGGCGAACACCGCTCCTCCTGCTCGCCCTCTAGAGGCATGGGCGTCTTTAGGAC
 3096 BGL2,
 ArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyrAsnPro

FIGURE 18 - Page 6

3122 CGGAAGTCTCGGAGATTGCCCCAGGCCCTGCCCGTTTGGGCGCGGCCGGACTATAACCCC
GCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGGCCTGATATTGGGG
3143 ALWN1, 3164 EAG1 XMA3,
ProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGlyCysPro
3182 CCGCTAGTGGAGACGTGGAAAAAGCCCCGACTACGAACCACCTGTGGTCCATGGCTGCCCG
GGCGATCACCTCTGCACCTTTTCGGGGCTGATGCTTGGTGGACACCAGGTACCGACGGGC
3217 HGIE2, 3229 NCOI,
LeuProProProLysSerProProValProProProArgLysLysArgThrValValLeu
3242 CTTCCACCTCCAAAGTCCCCTCCTGTGCCTCCGCCTCGGAAGAAGCGGACGGTGGTCTC
GAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTTCGCCTGCCACCAGGAG
ThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGlySerSer
3302 ACTGAATCAACCCTATCTACTGCCTTGGCCGAGCTCGCCACCAGAAGCTTTGGCAGCTCC
TGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCGTCGAGG
3332 SAC1, 3346 HIND3,
SerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaProSerGly
3362 TCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCTTCTGGC
AGTTGAAGGCCGTAATGCCCCGCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGAAGACCG
CysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGlyGluPro
3422 TGCCCCCCCCGACTCCGACGCTGAGTCTATTCTCCATGCCCCCCTGGAGGGGGAGCCT
ACGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCCCTCGGA
3437 EAM11051,
GlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsnAlaGlu
3482 GGGGATCCGGATCTTAGCGACGGGTGATGGTCAACGGTCAGTAGTGAGGCCAACGCGGAG
CCCCTAGGCCTAGAATCGCTGCCCAGTACCAGTTGCCAGTCATCACTCCGGTTGCGCCTC
3484 BAMHI, 3485 BSAB1, 3487 BSPE1,
AspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrProCysAla
3542 GATGTCGTGTGCTGCTCAATGTCTTACTCTTGACAGGCGCACTCGTCACCCCGTGCGCC
CTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCGCGTGAGCAGTGGGGCACGCGG
3589 DRA3, 3600 SAC2,
AlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHisHisAsn
3602 GCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTCACCACAAT
CGCCTTCTTGTCTTTGACGGGTAGTTACGTGATTGTTGAGCAACGATGCAGTGGTGTTA
3611 ALWN1, 3655 PFLM1,
LeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThrPheAsp
3662 TTGGTGTATTCCACCACCTCACGCAGTGTGTCGCAAAGGCAGAGAAAGTCACATTGAC
AACCACATAAGGTGGTGGAGTGCCTCAGCAACGGTTTCCGCTTCTTTTCAGTGTAACCTG
3681 DRA3,
ArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAlaAlaAla
3722 AGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCAGCGGCG

FIGURE 18 - Page 7

TCTGACGTTCAAGACCTGTCGGTAATGGTCTCGCATGAGTTCCTCCAATTTCTGTCGCGGC

SerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrProProHis
 3782 TCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGCAGCCTGACGCCCCACAC
 AGTTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTCGGACTGCGGGGGTGTG

3816 HIND3,

SerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArgLysAla
 3842 TCAGCCAAATCCAAGTTTGGTTATGGGGCAAAGACGTCCGTTGCCATGCCAGAAAGGCC
 AGTCGGTTTAGGTTCAAACCAATACCCCGTTTTCTGCAGGCAACGGTACGGTCTTTCCGG

3875 AAT2, 3890 BGLI,

ValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrProIleAsp
 3902 GTAACCCACATCAACTCCGTGTGGAAAGACCTTCTGGAAGACAATGTACACCAATAGAC
 CATTGGGTGTAGTTGAGGCACACCTTCTGGAAGACCTTCTGTTACATTGTGGTTATCTG

ThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGlyArgLys
 3962 ACTACCATCATGGCTAAGAACGAGGTTTTCTGCGTTCAGCCTGAGAAGGGGGTTCGTAG
 TGATGGTAGTACCGATTCTTGCTCCAAAAGACGCAAGTCGGACTCTTCCCCCAGCATTC

ProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMetAlaLeu
 4022 CCAGTCGTCTCATCGTGTTCCTCGATCTGGGCGTGCAGCTGTGCGAAAAGATGGCTTTG
 GGTGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACACGCTTTTCTACCGAAAC

TyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPheGlnTyr
 4082 TACGACGTGGTTACAAAGCTCCCTTGGCCGTGATGGGAAGCTCCTACGGATTCCAATAC
 ATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCTTCGAGGATGCCTAAGGTTATG

SerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThrProMet
 4142 TCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGGAAGTCCAAGAAAACCCCAATG
 AGTGGTCCTGTGCCCCAATTAAAGGAGCAGCTTCGCACCTTCAGGTTCTTTTGGGGTTAC

4160 ECORI,

GlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIleArgThr
 4202 GGGTTCTCGTATGATACCCGCTGCTTTGACTCCACAGTCACTGAGAGCGACATCCGTACG
 CCAAAGAGCATACTATGGGCGACGAACTGAGGTGTGAGTCACTCTCGCTGTAGGCATGC

4229 DRD1, 4236 ALWN1,

GluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIleLysSer
 4262 GAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCAAGCCCGCTGGCCATCAAGTCC
 CTCCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTTCGGCGCACCGGTAGTTCAGG

4301 BGLI, 4308 BALI,

LeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsnCysGly
 4322 CTCACCGAGAGGCTTTATGTTGGGGGCCCTTACCAATTCAAGGGGGGAGAACTGCGGC
 GAGTGGCTCTCCGAAATACAACCCCGGGGAGAATGGTTAAGTCCCCCTCTTGACGCCG

4345 APAI,

TyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeuThrCys
 4382 TATCGCAGGTGCCGCGGAGCGGCGTACTGACAACCTAGCTGTGGTAACACCCTCACTTGC
 ATAGCGTCCACGGCGCGCTCGCCGCATGACTGTTGATCGACACCATTGTGGGAGTGAACG

FIGURE 18 - Page 8

TyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMetLeuVal
 4442 TACATCAAGGCCCGGGCAGCCTGTCGAGCCGCAGGGCTCCAGGACTGCACCATGCTCGTG
 ATGTAGTTCCGGGCGGTCGGACAGCTCGGCGTCCCGAGGTCCTGACGTGGTACGAGCAC
 ^
 4452 SMAI XMAI,
 CysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAlaAlaSer
 4502 TGTGGCGACGACTTAGTCGTTATCTGTGAAAGCGCGGGGTCCAGGAGGACGCGGCGAGC
 ACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCTCCTGCGCCGCTCG
 ^ ^
 4508 DRD1, 4511 TTH3I,
 LeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspProProGln
 4562 CTGAGAGCCTTCACGGAGGCTATGACCAGGTACTCCGCCCCCTGGGGACCCCCACAA
 GACTCTCGGAAGTGCTCCGATACTGGTCCATGAGGCGGGGGGACCCCTGGGGGTGTT
 ProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAlaHisAsp
 4622 CCAGAATACGACTTGGAGCTCATAACATCATGCTCCTCCAACGTGTCAGTCGCCCACGAC
 GGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGGGTGCTG
 ^
 4637 SACI,
 GlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAlaArgAla
 4682 GCGCTGGAAAGAGGGTCTACTACCTCACCCGTGACCCTACAACCCCTCGCGAGAGCT
 CCGCGACCTTTCTCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGAGCGCTCTCGA
 ^
 4731 NRUI,
 AlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIleMetPhe
 4742 GCGTGGGAGACAGCAAGACACACTCCAGTCAATTCCTGGCTAGGCAACATAATCATGTTT
 CGCACCCCTCTGTCGTTCTGTGTGAGGTCAGTTAAGGACCGATCCGTTGTATTAGTACAAA
 AlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeuIleAla
 4802 GCCCCACACTGTGGGCGAGGATGATACTGATGACCCATTTCTTTAGCGTCCTTATAGCC
 CGGGGGTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAATATCGG
 ^ ^
 4806 PFLM1, 4807 DRA3,
 ArgAspGlnLeuGluGlnAlaLeuAspCysGluIleTyrGlyAlaCysTyrSerIleGlu
 4862 AGGGACCAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCCTGCTACTCCATAGAA
 TCCCTGGTCGAACTTGTCCGGGAGCTAACGCTCTAGATGCCCCGGACGATGAGGTATCTT
 ^
 4893 BGL2,
 ProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSerLeuHis
 4922 CCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTTCACTCCAC
 GGTGACCTAGATGGAGGTTAGTAAGTTTCTGAGGTACCGAGTCGCGTAAAAGTGAGGTG
 ^
 4954 NCOI,
 SerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGlyValPro
 4982 AGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGCATGCCTCAGAAAATTTGGGGTACCG
 TCAATGAGAGGTCCACTTTAGTTATCCCACGGCGTACGGAGTCTTTTGAACCCCATGGC
 ^ ^
 5015 SPHI, 5035 KPNI,

FIGURE 18 - Page 9

ProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAlaArgGly
 5042 CCCTTGCAGCTTGGAGACACCGGGCCCGGAGCGTCCGCGCTAGGCTTCTGGCCAGAGGA
 GGAACGCTCGAACCTCTGTGGCCCGGCCTCGCAGGCGCGATCCGAAGACCGGTCTCCT
 ^ ^ ^
 5064 APAI, 5091 BALI,
 GlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLysLeuLys
 5102 GGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAGCTCAAA
 CCGTCCCGACGGTATACACCGTTTCATGGAGAAGTTGACCCGTCATTCTTGTTCGAGTTT
 ^
 5113 NDEI,
 LeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAlaGlyTyr
 5162 CTCACTCCAATAGCGGCCGCTGGCCAGCTGGACTTGTCCGGCTGGTTCACGGCTGGCTAC
 GAGTAGGTTATCGCCGCGGACCGGTTCGACCTGAACAGGCCGACCAAGTCCCGACCGATG
 ^ ^ ^ ^
 5174 NOTI, 5175 EAGI XMA3, 5182 BALI, 5186 PVU2,
 SerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrpPheCys
 5222 AGCGGGGAGACATTTATCACAGCGTGTCTCATGCCCGGCCCGCTGGATCTGGTTTTGC
 TCGCCCCCTCTGTAAATAGTGTGCGACAGAGTACGGGCCGGGGCGACCTAGACCAAAACG
 ^
 5240 DRA3,
 LeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgMetSerThrAsn
 5282 CTACTCTGCTTGCTGCAGGGGTAGGCATCTACCTCCTCCCCAACCGAATGAGCACGAAT
 GATGAGGACGAACGACGTCCCCATCCGTAGATGGAGGAGGGGTGGCTTACTCGTGCTTA
 ^
 5295 PSTI,
 ProLysProGlnArgLysThrLysArgAsnThrAsnArgArgProGlnAspValLysPhe
 5342 CCTAAACCTCAAAGAAAGACCAACGTAACACCAACCGGCGCGCAGGACGTCAAGTTC
 GGATTTGGAGTTTCTTTCTGGTTTGCATTGTGGTTGGCCGCGCGCGTCTGCAGTTCAAG
 ^ ^ ^ ^
 5380 NOTI, 5381 EAGI XMA3, 5390 AAT2, 5401 SMAI XMAI,
 ProGlyGlyGlyGlnIleValGlyGlyValTyrLeuLeuProArgArgGlyProArgLeu
 5402 CCGGTGGCGGTGATCGTTGGTGGAGTTTACTTGTGTCGCGCAGGGGCCCTAGATTG
 GGCCACCGCCAGTCTAGCAACCACCTCAAATGAACAACGGCGCGTCCCCGGGATCTAAC
 ^
 5449 APAI,
 GlyValArgAlaThrArgLysThrSerGluArgSerGlnProArgGlyArgArgGlnPro
 5462 GGTGTGCGCGCAGCAGAAAGACTTCCGAGCGGTGCGAACCTCGAGGTAGACGTACGCCT
 CCACACGCGCGTCTCTTTCTGAAGGCTCGCCAGCGTTGGAGCTCCATCTGCAGTCGGA
 ^ ^ ^ ^
 5467 BSSH2, 5478 XMNI, 5502 XHOI, 5511 AAT2,
 IleProLysAlaArgArgProGluGlyArgThrTrpAlaGlnProGlyTyrProTrpPro
 5522 ATCCCCAAGGCTCGTCGCCCCGAGGGCAGGACCTGGGCTCAGCCCGGGTACCCTTGGCCC
 TAGGGGTTCCGAGCAGCCGGGCTCCCGTCTGGACCCGAGTCGGGCCCATGGGAACCGGG
 ^ ^ ^ ^
 5548 ALWN1, 5558 ESP1, 5564 SMAI XMAI, 5568 KPNI,
 LeuTyrGlyAsnGluGlyCysGlyTrpAlaGlyTrpLeuLeuSerProArgGlySerArg
 5582 CTCTATGGCAATGAGGGCTGCGGGTGGGCGGGATGGCTCCTGTCTCCCCGTGGCTCTCGG
 GAGATACCGTTACTCCCGACGCCACCCGCCCTACCGAGGACAGAGGGGCACCGAGAGCC

FIGURE 18 - Page 10

ProSerTrpGlyProThrAspProArgArgArgSerArgAsnLeuGlyLysValIleAsp
5642 CCTAGCTGGGGCCCCACAGACCCCGGCGTAGGTCGCGCAATTGGGTAAGGTCATCGAT
GGATCGACCCCGGGGTGTCTGGGGCCGCATCCAGCGGTTAAACCCATTCCAGTAGCTA
5650 APAI, 5696 CLAI,
ThrLeuThrCysGlyPheAlaAspLeuMetGlyTyrIleProLeuValGlyAlaProLeu
5702 ACCCTTACGTGCGGCTTCGCCGACCTCATGGGGTACATACCGCTCGTCGGCGCCCCTCTT
TGGAATGCACGCCGAAGCGGCTGGAGTACCCCATGTATGGCGAGCAGCCGCGGGGAGAA
5724 HGIE2, 5750 KAS1 NARI, 5756 ECON1,
GlyGlyAlaAlaArgAlaLeuAlaHisGlyValArgValLeuGluAspGlyValAsnTyr
5762 GGAGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCGGGTTCTGGAAGACGGCGTGAACCTAT
CCTCCGCGACGGTCCCGGGACCGGTACCGCAGGCCCAAGACCTTCTGCCGCACTTGATA
5772 BSTXI, 5775 APAI,
AlaThrGlyAsnLeuProGlyCysSerOC AM
5822 GCAACAGGGAACCTTCCTGGTTGCTCTTAATAGTCGAC
CGTTGTCCCTTGGAAGGACCAACGAGAATTATCAGCTG
5854 SALI,

FIGURE 19

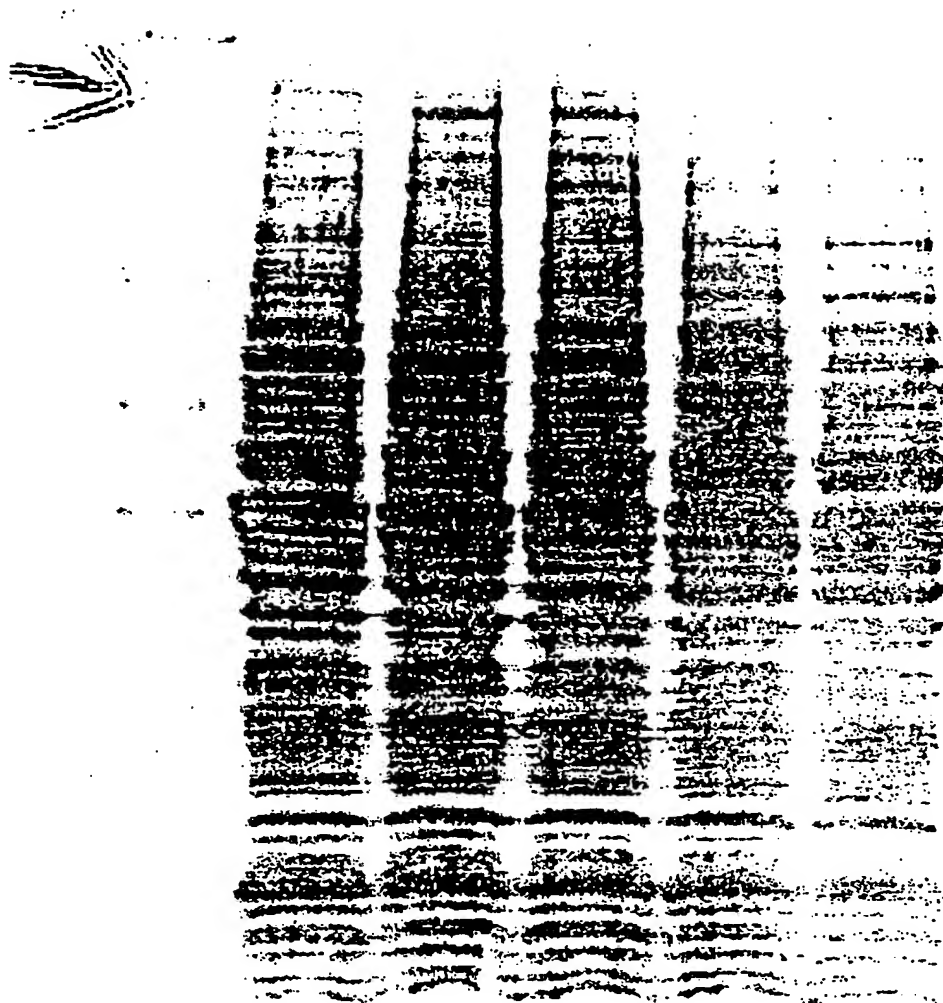


FIGURE 20 - Page 1

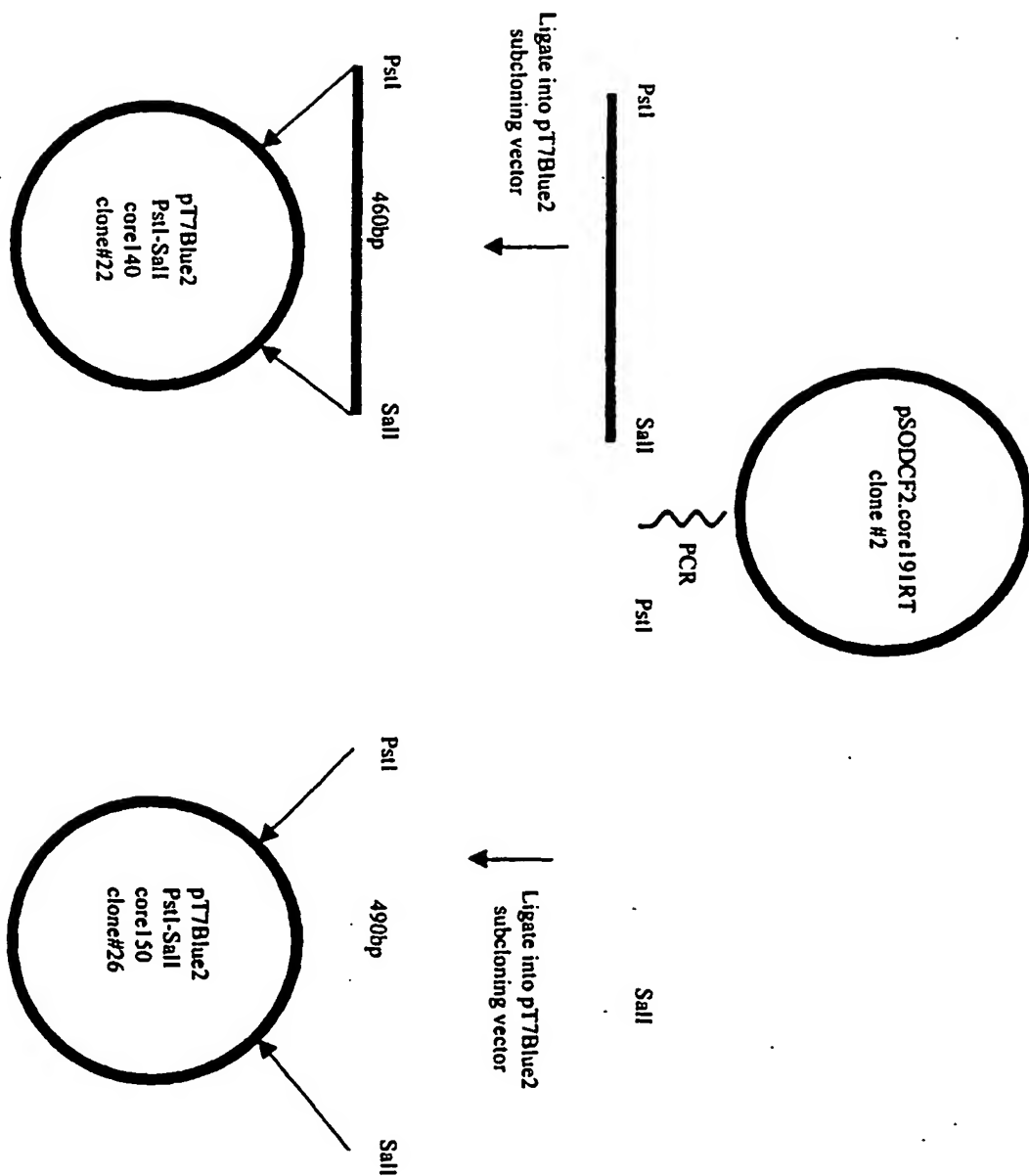


FIGURE 20 - Page 2

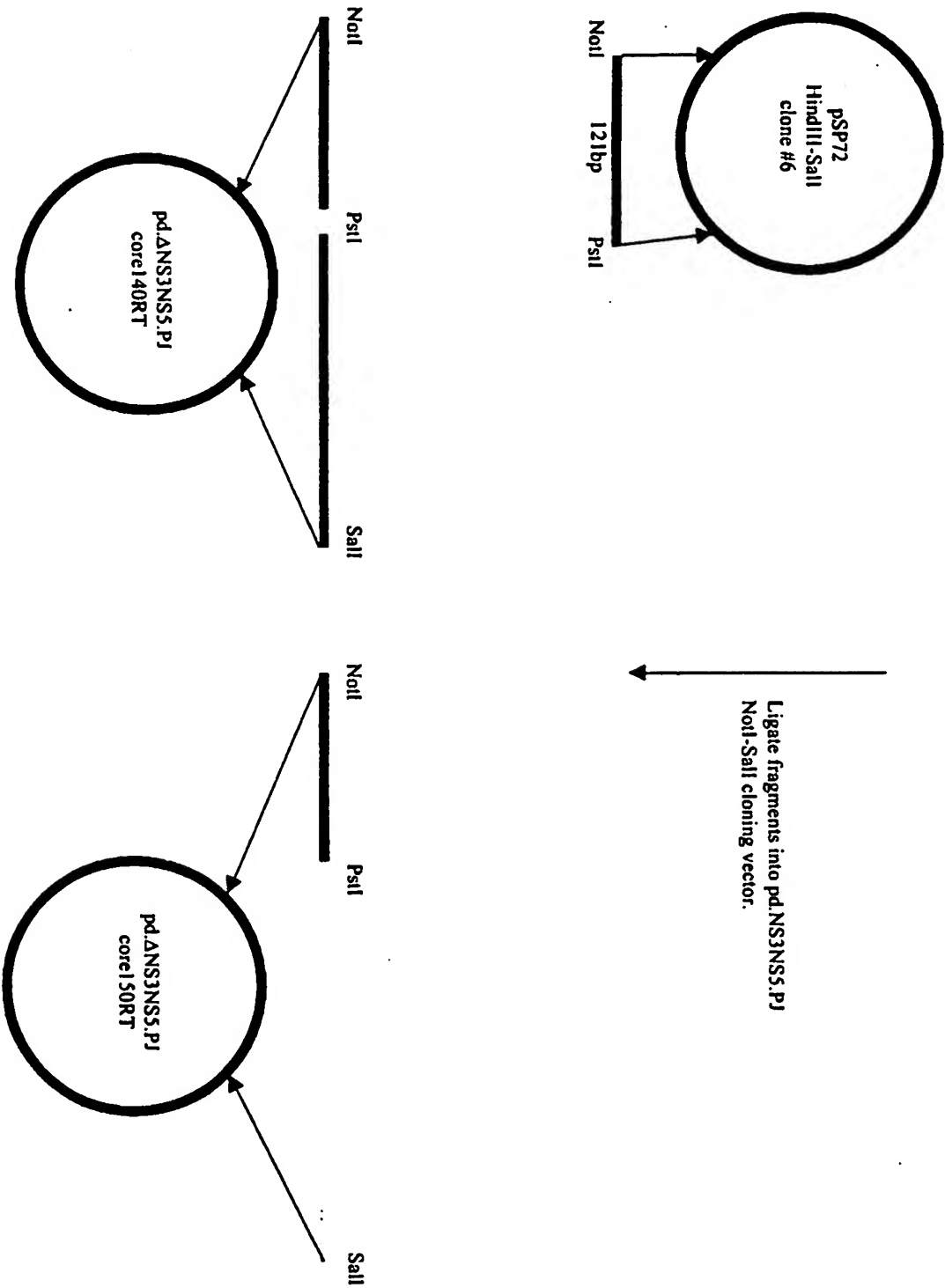


FIGURE 21 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuValLeuAsn
2 AGCTTACAAAACAAAATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTACTCAAC
TCGAATGTTTTGTTTTACCGACGTATACGTCGAGTCCCGATATTCCACGATCATGAGTTG
^ ^ ^
1 HIND3, 24 NDEI, 52 SCAI,

ProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGlyIleAsp
62 CCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGGATCGAT
GGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCCTAGCTA
^
116 CLAI,

ProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyrSerThr
122 CCTAACATCAGGACCGGGGTGAGAACAAATTACCACTGGCAGCCCCATCACGTACTCCACC
GGATTGTAGTCCTGGCCCCACTTTGTTAATGGTGACCGTCGGGGTAGTGCATGAGGTGG

TyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIleIleCys
182 TACGGCAAGTTCCTTGCCGACGGCGGGTGCTCGGGGGGCGCTTATGACATAATAATTGT
ATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGCAATACTGTATTATTAACA

AspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeuAspGln
242 GACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGTCCTTGACCAA
CTGCTCACGGTGAGGTGCCTACGGTGTAGGTAGAACCCGTAACCGTGACAGGAAGTGGTT

AlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGlySerVal
302 GCAGAGACTGCGGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGCTCCGTC
CGTCTCTGACGCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGAGGCCGAGGCAG
^
303 ALWN1,

ThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIleProPhe
362 ACTGTGCCCCATCCCAACATCGAGGAGGTTGCTCTGTCCACCACCGGAGAGATCCCTTTT
TGACACGGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAGGGAAAA

TyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePheCysHis
422 TACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTCTGTCAT
ATGCCGTTCCGATAGGGGGAGCTTCATTAGTTCCCCCCTCTGTAGAGTAGAAGACAGTA

FIGURE 21 - Page 2

SerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsnAlaVal
 482 TCAAAGAAGAAGTGCGACGAACCTCGCCGAAAGCTGGTCGCATTGGGCATCAATGCCGTG
 AGTTTCTTCTTCACGCTGCTTGAGCGGCGTTTCGACCAGCGTAACCCGTAGTTACGGCAC
 AlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValValValVal
 542 GCCTACTACCGCGGTCTTGACGTGTCCGTCATCCCGACCAGCGGCGATGTTGTCTGTCGTG
 CGGATGATGGCGCCAGAAGTGCACAGGCAGTAGGGCTGGTCGCCGCTACAACAGCAGCAC
 550 SAC2, 560 DRD1,
 AlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAspCysAsn
 602 GCAACCGATGCCCTCATGACCGGCTATACCGGCGACTTCGACTCGGTGATAGACTGCAAT
 CGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTGACGTTA
 615 BSPH1,
 ThrCysValThrGlnThrValAspPheSerLeuAspProThrPheThrIleGluThrIle
 662 ACGTGTGTACCCAGACAGTCGATTTCAGCCTTGACCCTACCTTCACCATTGAGACAATC
 TGCACACAGTGGGTCTGTCTAGCTAAAGTCGGAAGTGGGATGGAAGTGGTAACTCTGTTAG
 ThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArgGlyLys
 722 ACGCTCCCCAAGATGCTGTCTCCCGCACTCAACGTCGGGGCAGGACTGGCAGGGGGAAG
 TGCAGAGGGGGTTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCCTGACCGTCCCCCTTC
 ProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAspSerSer
 782 CCAGGCATCTACAGATTTGTGGCACCAGGGGAGCGCCCCCTCCGGCATGTTTCGACTCGTCC
 GGTCGGTAGATGTCTAAACACCGTGGCCCCCTCGCGGGGAGGCCGTACAAGCTGAGCAGG
 816 BGLI, 833 DRD1,
 ValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAlaGluThr
 842 GTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTCAGCCCCGCCGAGACT
 CAGGAGACACTACGATACTGCGTCCGACACGAACCATACTCGAGTGGGGGCGGCTCTGA
 881 SACI,
 ThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAspHisLeu
 902 ACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGACCATCTT
 TGCAATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCCTGGTAGAA
 931 SMAI XMAI,
 GluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeuSerGln
 962 GAATTTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTATCCAG
 CTTAAAACCCCTCCCGCAGAAATGTCGGGAGTGAGTATATCTACGGGTGAAAGATAGGGTC
 985 STUI,
 ThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrValCysAla
 1022 ACAAGCAGAGTGGGGAGAACCTTCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCT
 TGTTTCGTCTACCCCTCTTGAAGGAATGGACCATCGCATGGTTCGGTGGCACACGCCA
 1069 DRA3,
 ArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArgLeuLys
 1082 AGGGCTCAAGCCCCCTCCCCATCGTGGGACCAGATGTGAAGTGTGTTGATTGCGCTCAAG

FIGURE 21 - Page 3

TCCCGAGTTCGGGGAGGGGGTAGCACCCTGGTCTACACCTTCACAACTAAGCGGAGTTC

ProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsnGluIle
 1142 CCCACCCTCCATGGGCCAACCCCCTGCTATACAGACTGGGCGCTGTTCAGAAATGAAATC
 GGGTGGGAGGTACCCGGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTACTTTAG
 1150 NCOI,

ThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeuGluVal
 1202 ACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTGGAGGTC
 TGGGACTGCGTGGGTCA GTGGTTTATGTAGTACTGTACGTACAGCCGGCTGGACCTCCAG
 1230 BSPH1, 1234 DRD1, 1237 AVA3, 1245 EAG1 XMA3, 1250 DRD1,

ValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyrCysLeu
 1262 GTCACGAGCACCTGGGTGCTCGTTGGCGGCGTCCTGGCTGCTTTGGCCGCGTATTGCCTG
 CAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATAACGGAC

SerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAlaIleIle
 1322 TCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCGGGAAGCCGGCAATCATA
 AGTTGTCCGACGCACCAGTATCACCCGTCCCAGCAGAACAGGCCCTTCGGCCGTTAGTAT
 1369 NAEI,

ProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGlnHisLeu
 1382 CCTGACAGGGAAGTCCTCTACCGAGAGTTCGATGAGATGGAAGAGTGCTCTCAGCACTTA
 GGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCACGAGAGTCGTGAAT
 1385 DRD1,

ProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeuGlyLeu
 1442 CCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTC AAGCAGAAGGCCCTCGGCCTC
 GGCATGTAGCTCGTTCCTACTACGAGCGGCTCGTCAAGTTCGTCTTCCGGGAGCCGGAG

LeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsnTrpGln
 1502 CTGCAGACCGCGTCCCGTCAGGCAGAGTTATCGCCCTGCTGTCCAGACCAACTGGCAA
 GACGTCTGGCGCAGGGCAGTCCGTCTCCAATAGCGGGGACGACAGGTCTGGTTGACCGTT
 1502 PSTI, 1507 TTH3I,

LysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGlnTyrLeu
 1562 AAACCTCGAGACCTTCTGGGCGAAGCATATGTGGAACCTCATCAGTGGGATACAATACTTG
 TTTGAGCTCTGGAAGACCCGCTTCGTATACACCTTGAAGTAGTCACCTATGTTATGAAC
 1565 XHOI, 1586 NDEI,

AlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPheThrAla
 1622 GCGGGCTTGTCAACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTTACAGCT
 CGCCCGAACAGTTGCGACGGACCATTTGGGGCGGTAACGAAGTAAC TACCGAAATGTCGA
 1643 BSTE2, 1677 ALWN1 PVU2,

AlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGlyGlyTrp
 1682 GCTGTCAACAGCCCACTAACCCTAGCCAAACCCCTCTTCAACATATTGGGGGGGTGG
 CGACAGTGGTCGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCCCCCACC

FIGURE 21 - Page 4

ValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGlyLeuAla
 1742 GTGGCTGCCCAGCTCGCCGCCCGCGGTGCCGCTACTGCCTTTGTGGGCGCTGGCTTAGCT
 CACCGACGGGTCGAGCGGGCGGGGCCACGGCGATGACGGAAACACCCGCGACCGAATCGA
 1794 ESP1,
 GlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAlaGlyTyr
 1802 GCGCCGCCATCGGCAGTGTGGACTGGGAAGGTCCTCATAGACATCCTTGCAGGGTAT
 CCGCGGGCGGTAGCCGTCACAACCTGACCCCTTCCAGGAGTATCTGTAGGAACGTCCATA
 1802 KAS1 NARI,
 GlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluValProSer
 1862 GCGCGGGCGGTGGCGGGAGCTCTTGTGGCATTCAAGATCATGAGCGGTGAGGTCCCCTCC
 CCGCGCCCGCACCGCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAGGGGAGG
 1878 SACI, 1899 BSPH1,
 ThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuValValGly
 1922 ACGGAGGACCTGGTCAATCTACTGCCCGCCATCCTCTCGCCCGGAGCCCTCGTAGTCGGC
 TGCTCTCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGGCCTCGGGAGCATCAGCCG
 1928 TTH3I,
 ValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaValGlnTrp
 1982 GTGGTCTGTGCAGCAATACTGCGCCGGCACGTTGGCCCGGGCGAGGGGGCAGTGCAGTGG
 CACCAGACACGTCGTTATGACGCGGGCGGTGAACCGGGCCCGCTCCCCCGTCACGTCACC
 2004 NAEI, 2017 SMAI XMAI,
 MetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal
 2042 ATGAACCGGCTGATAGCCTTCGCCTCCCGGGGAACCATGTTTCCCCCACGCACTACGTG
 TACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGTGCGTGATGCAC
 2067 SMAI XMAI, 2093 DRA3,
 ProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrValThrGln
 2102 CCGGAGAGCGATGCAGCTGCCCGCGTCACTGCCATACTCAGCAGCCTCACTGTAACCCAG
 GGCCTCTCGCTACGTGACGGGCGCAGTGACGGTATGAGTCGTCGGAGTGACATTGGGTC
 2115 PVU2, 2159 ALWN1,
 LeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSerGlySer
 2162 CTCCTGAGGCGACTGCACCACTGGATAAGCTCGGAGTGTACCACTCCATGCTCCGGTTCC
 GAGGACTCCGCTGACGTGGTCACTATTTCGAGCCTCACATGGTGAGGTACGAGGCCAAGG
 2164 MST2, 2220 ECON1,
 TrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThrTrpLeu
 2222 TGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACCTGGCTA
 ACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGGACCGAT
 LysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArgGlyTyr
 2282 AAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCCTTTGTGTCCTGCCAGCGCGGGTAT
 TTTGATTTCGAGTACGGTGTGACGGACCCCTAGGGGAAACACAGGACGGTCGCGCCCAT
 2285 ESP1, 2300 PVU2, 2310 BAMHI,

FIGURE 21 - Page 5

LysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAlaGluIle
2342 AAGGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGCTGCCACTGTGGAGCTGAGATC
TTCCCCCAGACCGTCTCCCTGCCGTAGTACGTGTGAGCGACGGTGACACCTCGACTCTAG

ThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArgAsnMet
2402 ACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCTTAGGACCTGCAGGAACATG
TGACCTGTACAGTTTTTGGCCCTGACTCCTAGCAGCCAGGATCCTGGACGTCTTGTA

2425 BSAB1, 2441 AVR2, 2448 SSE83871, 2449 PSTI,

TrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeuProAla
2462 TGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGCCCCCTGTACCCCCCTTCTGCG
ACCTCACCCTGGAAGGGGTAATTACGGATGTGGTGCCCGGGGACATGGGGGGAAGGACGC

2480 ASE1, 2497 APAI,

ProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIleArgGln
2522 CCGAACTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATAAGGCAG
GGCTTGATGTGCAAGCGCGATACCTCCCACAGACGTCTCCTTATGCACCTCTATTCCGTC

2553 PSTI,

ValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysProCysGln
2582 GTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCCGTGCCAG
CACCCCCTGAAGGTGATGCACCTGCCCATACTGATGACTGTTAGAAATTTACGGGCACGGTC

2594 DRA3,

ValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPheAlaPro
2642 GTCCCATCGCCGAATTTTTACAGAATTGGACGGGGTGCCTACATAGGTTTGCGCCC
CAGGGTAGCGGGCTTAAAAAGTGCTTAACCTGCCCCACGCGGATGTATCCAAACGCGGG

ProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGluTyrPro
2702 CCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTCAGAGTAGGACTCCACGAATACCCG
GGGACGTTTCGGGAACGACGCCCTCTCCATAGTAAGTCTCATCCTGAGGTGCTTATGGGC

2757 HGIE2,

ValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSerMetLeu
2762 GTAGGGTTCGCAATTACCTTGCGAGCCCGAACCGACGTGGCCGTGTTGACGTCCATGCTC
CATCCCAGCGTTAATGGAACGCTCGGGCTTGCGCTGCACCGGCACAACATGCAGGTACGAG

2809 AAT2,

ThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGlySerPro
2822 ACTGATCCCTCCCATATAACAGCAGAGGCGGCCGGGCGAAGGTTGGCGAGGGGATCACCC
TGACTAGGGAGGGTATATTGTCGTCTCCGCGGCCCGCTTCCAACCGCTCCCTAGTGGG

2850 EAG1 XMA3,

ProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAlaThrCys
2882 CCCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCAACTTGC
GGGAGACACCGGTTCGAGGAGCGGATCGGTTCGATAGGCGAGGTAGAGAGTTCCGTTGAACG

2889 BALI, 2903 NHEI,

FIGURE 21 - Page 6

ThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrpArgGln
 2942 ACCGCTAACCATGACTCCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGGAGGCAG
 TGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGGTTGGAGGATACCTCCGTC
 ^ ^
 2966 ESP1, 2969 SACI,
 GluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeuAspSer
 3002 GAGATGGGCGGCAACATCACCAGGGTTGAGTCAGAAAACAAAGTGGTGATTCTGGACTCC
 CTCTACCCGCCGTTGTAGTGGTCCCACTCAGTCTTTTGTTCACCACTAAGACCTGAGG
 PheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGluIleLeu
 3062 TTCGATCCGCTTGTGGCGGAGGAGGACGAGCGGGAGATCTCCGTACCCGCAGAAATCCTG
 AAGCTAGGCGAACACCGCCTCCTCCTGCTCGCCCTCTAGAGGCATGGGCGTCTTTAGGAC
 ^
 3096 BGL2,
 ArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyrAsnPro
 3122 CGGAAGTCTCGGAGATTGCCCCAGGCCCTGCCCGTTTGGGCGCGGCCGACTATAACCCC
 GCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGCGCTGATATTGGGG
 ^ ^
 3143 ALWN1, 3164 EAG1 XMA3,
 ProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGlyCysPro
 3182 CCGCTAGTGGAGACGTGGAAAAAGCCGACTACGAACACCTGTGGTCCATGGCTGCCCG
 GGCGATCACCTCTGCACCTTTTCGGGCTGATGCTTGGTGGACACCAGGTACCGACGGGC
 ^ ^
 3217 HGIE2, 3229 NCOI,
 LeuProProProLysSerProProValProProProArgLysLysArgThrValValLeu
 3242 CTTCCACCTCCAAAGTCCCCTCCTGTGCCTCCGCCTCGGAAGAAGCGGACGGTGGTCTC
 GAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTCGCCTGCCACCAGGAG
 ThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGlySerSer
 3302 ACTGAATCAACCCTATCTACTGCCTTGGCCGAGCTCGCCACCAGAAGCTTTGGCAGCTCC
 TGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCGTCGAGG
 ^ ^
 3332 SACI, 3346 HIND3,
 SerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaProSerGly
 3362 TCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCTTCTGGC
 AGTTGAAGGCCGTAATGCCCGCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGAAGACCG
 CysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGlyGluPro
 3422 TGCCCCCGGACTCCGACGCTGAGTCTATTCTCCTCCATGCCCCCCTGGAGGGGGAGCCT
 ACGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCCCTCGGA
 ^
 3437 EAM11051,
 GlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsnAlaGlu
 3482 GGGGATCCGGATCTTAGCGACGGGTCAAGGTCAGTAGTGAGGCCAACCGGGAG
 CCCCTAGGCCTAGAATCGCTGCCAGTACCAGTTGCCAGTCATCACTCCGGTTGCGCCTC
 ^ ^ ^
 3484 BAMHI, 3485 BSAB1, 3487 BSPE1,
 AspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrProCysAla
 3542 GATGTCGTGTGCTGCTCAATGTCTTACTCTTGGACAGGCGCACTCGTCACCCCGTGCGCC
 CTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCGCGTGAGCAGTGGGGCACGGG

FIGURE 21 - Page 7

3589 DRA3, 3600 SAC2,

3602 AlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHisHisAsn
GCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTCACCACAAT
CGCCTTCTTGCTTTGACGGGTAGTTACGTGATTGTTGAGCAACGATGCAGTGGTGTTA
^ ^

3611 ALWN1, 3655 PFLM1,

3662 LeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThrPheAsp
TTGGTGTATTCCACCACCTCACGCAGTGCTTGCCAAAGGCAGAAGAAAGTCACATTTGAC
AACCACATAAGGTGGTGGAGTGCGTCACGAACGGTTTCCGTCTTCTTTCAGTGTAAGT
^

3681 DRA3,

3722 ArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAlaAlaAla
AGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCAGCGCG
TCTGACGTTCAAGACCTGTCGGTAATGGTCTGCATGAGTTCCTCAATTTCTGTCGCCG

3782 SerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrProProHis
TCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGACGCCTGACGCCCCACAC
AGTTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTGCGACTGCGGGGGTGTG
^

3816 HIND3,

3842 SerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArgLysAla
TCAGCCAAATCCAAGTTTGGTTATGGGGCAAAGACGTCCGTTGCCATGCCAGAAAGGCC
AGTCGGTTTAGGTTCAAACCAATACCCCGTTTTCTGCAGGCAACGGTACGGTCTTTCCGG
^ ^

3875 AAT2, 3890 BGLI,

3902 ValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrProIleAsp
GTAACCCACATCAACTCCGTGTGGAAAGACCTTCTGGAAGACAATGTAACACCAATAGAC
CATTGGGTGTAGTTGAGGCACACCTTTCTGGAAGACCTTCTGTACATTGTGGTTATCTG

3962 ThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGlyArgLys
ACTACCATCATGGCTAAGAACGAGGTTTTCTGCGTTGAGCCTGAGAAGGGGGGTGTAAG
TGATGGTAGTACCGATTCTTGCTCCAAAGACGCAAGTCGGACTCTTCCCCCAGCATTC

4022 ProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMetAlaLeu
CCAGCTCGTCTCATCGTGTTCCTCGATCTGGGCGTGCGCGTGTGCGAAAAGATGGCTTTG
GGTCGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACAGCTTTTCTACCGAAAC

4082 TyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPheGlnTyr
TACGACGTGGTTACAAAGCTCCCTTGGCCGTGATGGGAAGCTCCTACGGATTCCAATAC
ATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCTTCGAGGATGCCTAAGGTTATG

4142 SerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThrProMet
TCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGGAAGTCCAAGAAAACCCCAATG
AGTGGTCCTGTCGCCCACTTAAGGAGCAGTTCGCACCTTCAGGTTCTTTGGGGTTAC
^

4160 ECORI,

4202 GlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIleArgThr
GGGTTCTCGTATGATACCGCTGCTTTGACTCCACAGTCACTGAGAGCGACATCCGTACG
CCCAAGAGCATACTATGGGCGACGAACTGAGGTGTCAGTGACTCTCGCTGTAGGCATGC
^ ^

FIGURE 21 - Page 8

4229 DRD1, 4236 ALWN1,

4262 GluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIleLysSer
 GAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCAAGCCCGGTGGCCATCAAGTCC
 CTCCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTTCGGGCGCACCGGTAGTTCAGG
 ^ ^

4301 BGLI, 4308 BALI,

4322 LeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsnCysGly
 CTCACCGAGAGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAACTGCGGC
 GAGTGGCTCTCCGAAATACAACCCCGGGAGAATGGTTAAGTTCCTCCCTCTTGACGCCG
 ^

4345 APAI,

4382 TyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeuThrCys
 TATCGCAGGTGCCGCGGAGCGGCTACTGACAACTAGCTGTGGTAACACCCTCACTTGC
 ATAGCGTCCACGGCGGCTCGCCGCATGACTGTTGATCGACACCATTTGTGGGAGTGAACG

4442 TyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMetLeuVal
 TAATCAAGGCCCGGGCAGCCTGTCGAGCCGAGGGCTCCAGGACTGCACCATGCTCGTG
 ATGTAGTTCCGGGCCCGTCCGACAGCTCGGCGTCCCGAGGTCCTGACGTGGTACGAGCAC
 ^

4452 SMAI XMAI,

4502 CysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAlaAlaSer
 TGTGGCGACGACTTAGTCGTTATCTGTGAAAGCGCGGGGTCCAGGAGGACGCGGCGAGC
 ACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCTCTGCGCCGCTCG
 ^ ^

4508 DRD1, 4511 TTH3I,

4562 LeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspProProGln
 CTGAGAGCCTTCACGGAGGCTATGACCAGGTACTCCGCCCCCTGGGGACCCCCACAA
 GACTCTCGGAAGTGCTCCGATACTGGTCCATGAGGCGGGGGGACCCCTGGGGGTGTT

4622 ProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAlaHisAsp
 CCAGAATACGACTTGGAGCTCATAACATCATGCTCTCCAACGTGTCAGTCGCCCCACGAC
 GGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGGTGCTG
 ^

4637 SACI,

4682 GlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAlaArgAla
 GGCCTGGAAAGAGGTCTACTACCTCACCCGTGACCCTACAACCCCTCGCGAGAGCT
 CCGCGACCTTTCTCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGGAGCGCTCTCGA
 ^

4731 NRUI,

4742 AlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIleMetPhe
 GCGTGGGAGACAGCAAGACACACTCCAGTCAATTCTGGCTAGGCAACATAATCATGTTT
 CGCACCTCTGTCTTCTGTGTGAGGTGAGTTAAGGACCGATCCGTTGTATTAGTACAAA

4802 AlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeuIleAla
 GCCCCACACTGTGGGCGAGGATGATACTGATGACCCATTTCTTTAGCGTCCTTATAGCC
 CGGGGGTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAATATCGG
 ^ ^

4806 PFLM1, 4807 DRA3,

ArgAspGlnLeuGluGlnAlaLeuAspCysGluIleTyrGlyAlaCysTyrSerIleGlu

FIGURE 21 - Page

4862 AGGGACCAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCTGCTACTCCATAGAA-
TCCCTGGTCGAACCTGTCCGGGAGCTAACGCTCTAGATGCCCCGGACGATGAGGTATCTT
4893 BGL2,
ProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSerLeuHis
4922 CCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTTCACTCCAC
GGTGACCTAGATGGAGGTAGTAAGTTTCTGAGGTACCGGAGTCGCGTAAAAGTGAGGTG
4954 NCOI,
SerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGlyValPro
4982 AGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGATGCCTCAGAAAAGTTGGGGTACCG
TCAATGAGAGGTCCACTTTAGTTATCCCACCGGCGTACGGAGTCTTTTGAACCCCATGGC
5015 SPHI, 5035 KPNI,
ProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAlaArgGly
5042 CCCTTGGAGCTTGGAGACACCGGGCCGAGCGTCCGCGCTAGGCTTCTGGCCAGAGGA
GGGAACGCTCGAACCTCTGTGGCCCGGCGCTCGCAGGCGCGATCCGAAGACCGGTCTCCT
5064 APAI, 5091 BALI,
GlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLysLeuLys
5102 GGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAGCTCAA
CCGTCCCACGGTATACACCGTTCATGGAGAAGTTGACCCGTCATTCTTGTTTCGAGTTT
5113 NDEI,
LeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAlaGlyTyr
5162 CTCACCTCAATAGCGGCGCTGGCCAGCTGGACTTGTCCGGCTGGTTCACGGCTGGCTAC
GAGTGAGGTATCGCCGGCGACCGGTGACCTGAACAGGCCGACCAAGTGCCGACCGATG
5174 NOTI, 5175 EAGI XMA3, 5182 BALI, 5186 PVU2,
SerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrpPheCys
5222 AGCGGGGAGACATTTATCACAGCGTGTCTCATGCCCGCCCCGCTGGATCTGGTTTTGC
TCGCCCTCTGTAAATAGTGTGCGACAGAGTACGGGCGGGGCGACCTAGACCAAACG
5240 DRA3,
LeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgMetSerThrAsn
5282 CTACTCCTGCTTGCTGCAGGGGTAGGCATCTACCTCCTCCCAACCGAATGAGCACGAAT
GATGAGGACGAACGACGTCCCATCCGTAGATGGAGGAGGGGTGGCTTACTCGTGCTTA
5295 PSTI,
ProLysProGlnArgLysThrLysArgAsnThrAsnArgArgProGlnAspValLysPhe
5342 CCTAAACCTCAAAGAAAGACCAACGTAACACCAACCGCGCGCAGGACGTCAAGTTC
GGATTTGGAGTTTCTTTCTGGTTTGCATTGTGGTTGGCCGCGCGCTCCTGCAGTTCAAG
5380 NOTI, 5381 EAGI XMA3, 5390 AAT2, 5401 SMAI XMAI,
ProGlyGlyGlyGlnIleValGlyGlyValTyrLeuLeuProArgArgGlyProArgLeu
5402 CCGGTTGGCGGTGAGATCGTTGGTGGAGTTTACTTGTGCGCGCAGGGGCCCTAGATTG
GGCCACCGCCAGTCTAGCAACCACCTCAAATGAACAACGGCGCGTCCCGGGATCTAAC

FIGURE 21 - Page 10

5449 APAI,

GlyValArgAlaThrArgLysThrSerGluArgSerGlnProArgGlyArgArgGlnPro
 5462 GGTGTGCGCGCGACGAGAAAGACTTCCGAGCGGTCGCAACCTCGAGGTAGACGTCAGCCT
 CCACACGCGCGCTGCTCTTTCTGAAGGCTCGCCAGCGTTGGAGCTCCATCTGCAGTCGGA
 ^ ^ ^ ^ ^

5467 BSSH2, 5478 XMNI, 5502 XHOI, 5511 AAT2,

IleProLysAlaArgArgProGluGlyArgThrTrpAlaGlnProGlyTyrProTrpPro
 5522 ATCCCCAAGGCTCGTCGGCCCGAGGGCAGGACCTGGGCTCAGCCCGGGTACCCCTGGCCCC
 TAGGGGTTCCGAGCAGCCGGGCTCCCGTCTGGACCCGAGTCGGGCCCATGGGAACCGGG
 ^ ^ ^ ^ ^

5548 ALWN1, 5558 ESPI, 5564 SMAI XMAI, 5568 KPNI,

LeuTyrGlyAsnGluGlyCysGlyTrpAlaGlyTrpLeuLeuSerProArgGlySerArg
 5582 CTCTATGGCAATGAGGGCTGCGGGTGGGCGGGATGGCTCCTGTCTCCCCGTGGCTCTCGG
 GAGATACCGTTACTCCCGACGCCACCCGCCCTACCGAGGACAGAGGGGCACCGAGAGCC

ProSerTrpGlyProThrAspProArgArgArgSerArgAsnLeuGlyLysValIleAsp
 5642 CCTAGCTGGGGCCCCACAGACCCCGGCGTAGGTCGCGCAATTTGGGTAAGGTCATCGAT
 GGATCGACCCCGGGTGTCTGGGGGCCGCATCCAGCGCGTTAAACCCATTCCAGTAGCTA
 ^ ^ ^ ^ ^

5650 APAI, 5696 CLAI,

ThrLeuThrCysGlyPheAlaAspLeuMetGlyTyrIleProLeuValOC AM
 5702 ACCCTTACGTGCGGCTTCGCCGACCTCATGGGGTACATACCGCTCGTCTAATAGTCGAC
 TGGGAATGCACGCCGAAGCGGCTGGAGTACCCCATGTATGGCGAGCAGATTATCAGCTG
 ^ ^ ^ ^ ^

5724 HGIE2, 5755 SALI,

FIGURE 22 - Page 1

MetAlaAlaTyrAlaAlaGlnGlyTyrLysValLeuValLeuAsn
 2 AGCTTACAAAACAAAATGGCTGCATATGCAGCTCAGGGCTATAAGGTGCTAGTACTCAAC
 TCGAATGTTTTGTTTTACCGACGTATACGTCGAGTCCCGATATTCCACGATCATGAGTTG
 ^ ^ ^
 1 HIND3, 24 NDEI, 52 SCAI,

ProSerValAlaAlaThrLeuGlyPheGlyAlaTyrMetSerLysAlaHisGlyIleAsp
 62 CCCTCTGTTGCTGCAACACTGGGCTTTGGTGCTTACATGTCCAAGGCTCATGGGATCGAT
 GGGAGACAACGACGTTGTGACCCGAAACCACGAATGTACAGGTTCCGAGTACCCTAGCTA
 ^
 116 CLAI,

ProAsnIleArgThrGlyValArgThrIleThrThrGlySerProIleThrTyrSerThr
 122 CCTAACATCAGGACCGGGGTGAGAACAATTACCACTGGCAGCCCCATCAGTACTCCACC
 GGATTGTAGTCCTGGCCCCACTCTTGTTAATGGTGACCGTCGGGGTAGTGTCATGAGGTGG

TyrGlyLysPheLeuAlaAspGlyGlyCysSerGlyGlyAlaTyrAspIleIleIleCys
 182 TACGGCAAGTTCCTTGCCGACGGCGGGTGCTCGGGGGGCGCTTATGACATAATAATTTGT
 ATGCCGTTCAAGGAACGGCTGCCGCCACGAGCCCCCGCAATACTGTATTATTAAACA

AspGluCysHisSerThrAspAlaThrSerIleLeuGlyIleGlyThrValLeuAspGln
 242 GACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATTGGCACTGTCCTTGACCAA
 CTGCTCACGGTGAGGTGCCTACGGTGTAGGTAGAACCCGTAACCGTGACAGGAACCTGGTT

AlaGluThrAlaGlyAlaArgLeuValValLeuAlaThrAlaThrProProGlySerVal
 302 GCAGAGACTGCGGGGGCGAGACTGGTTGTGCTCGCCACCGCCACCCCTCCGGGCTCCGTC
 CGTCTCTGACGCCCCCGCTCTGACCAACACGAGCGGTGGCGGTGGGGAGGCCCGAGGCAG
 ^
 303 ALWN1,

ThrValProHisProAsnIleGluGluValAlaLeuSerThrThrGlyGluIleProPhe
 362 ACTGTGCCCCATCCCAACATCGAGGAGGTTGCTCTGTCCACCACCGGAGAGATCCCTTTT
 TGACACGGGGTAGGGTTGTAGCTCCTCCAACGAGACAGGTGGTGGCCTCTCTAGGGAAAA

TyrGlyLysAlaIleProLeuGluValIleLysGlyGlyArgHisLeuIlePheCysHis
 422 TACGGCAAGGCTATCCCCCTCGAAGTAATCAAGGGGGGAGACATCTCATCTTCTGTTCAT
 ATGCCGTTCCGATAGGGGGAGCTTCATTAGTTCCCCCCTCTGTAGAGTAGAAGACAGTA

FIGURE 22 - Page 2

SerLysLysLysCysAspGluLeuAlaAlaLysLeuValAlaLeuGlyIleAsnAlaVal
 482 TCAAAGAAGAAGTGCACGAACTCGCCGCAAAGCTGGTCGCATTGGGCATCAATGCCGTG
 AGTTTCTTCTTACGCTGCTTGAGCGGCGTTTCGACCAGCGTAACCCGTAGTTACGGCAC
 AlaTyrTyrArgGlyLeuAspValSerValIleProThrSerGlyAspValValValVal
 542 GCCTACTACCGCGGTCTTGACGTGTCCGTATCCCGACCAGCGCGATGTTGTCTCGTGTG
 CGGATGATGGCGCCAGAACTGCACAGGCAGTAGGGCTGGTCGCCGTACAACAGCAGCAC
 550 SAC2, 560 DRD1,
 AlaThrAspAlaLeuMetThrGlyTyrThrGlyAspPheAspSerValIleAspCysAsn
 602 GCAACCGATGCCCTCATGACCGGTATACCGGCGACTTCGACTCGGTGATAGACTGCAAT
 CGTTGGCTACGGGAGTACTGGCCGATATGGCCGCTGAAGCTGAGCCACTATCTGACGTTA
 615 BSPH1,
 ThrCysValThrGlnThrValAspPheSerLeuAspProThrPheThrIleGluThrIle
 662 ACGTGTGTACCCAGACAGTCGATTTTCAGCCTTGACCCTACCTTCACCATTGAGACAATC
 TGCACACAGTGGGTCTGTCTAGCTAAAGTCGGAAGTGGGATGGAAGTGGTAACCTCTGTTAG
 ThrLeuProGlnAspAlaValSerArgThrGlnArgArgGlyArgThrGlyArgGlyLys
 722 ACGTCCCCCAAGATGTCTCTCCGCACTCAACGTCCGGGCAGGACTGGCAGGGGGAAG
 TGCGAGGGGGTTCTACGACAGAGGGCGTGAGTTGCAGCCCCGTCTGACCGTCCCCCTTC
 ProGlyIleTyrArgPheValAlaProGlyGluArgProSerGlyMetPheAspSerSer
 782 CCAGGCATCTACAGATTTGTGGCACCAGGGGAGCGCCCCCTCCGGCATGTTTCGACTCGTCC
 GGTCCGTAGATGTCTAAACACCGTGGCCCCCTCGCGGGGAGGCCGTACAAGCTGAGCAGG
 816 BGLI, 833 DRD1,
 ValLeuCysGluCysTyrAspAlaGlyCysAlaTrpTyrGluLeuThrProAlaGluThr
 842 GTCCTCTGTGAGTGCTATGACGCAGGCTGTGCTTGGTATGAGCTACGCCCCCGGAGACT
 CAGGAGACACTCAGGATACTGCGTCCGACACGAACCATACTCGAGTGCAGGGCGGCTCTGA
 881 SACI,
 ThrValArgLeuArgAlaTyrMetAsnThrProGlyLeuProValCysGlnAspHisLeu
 902 ACAGTTAGGCTACGAGCGTACATGAACACCCCGGGGCTTCCCGTGTGCCAGGACCATCTT
 TGTCATCCGATGCTCGCATGTACTTGTGGGGCCCCGAAGGGCACACGGTCCTGGTAGAA
 931 SMAI XMAI,
 GluPheTrpGluGlyValPheThrGlyLeuThrHisIleAspAlaHisPheLeuSerGln
 962 GAATTTTGGGAGGGCGTCTTTACAGGCCTCACTCATATAGATGCCCACTTTCTATCCCAG
 CTTAAAACCTCCCGCAGAAATGTCCGGAGTGAGTATATCTACGGGTGAAAGATAGGGTC
 985 STUI,
 ThrLysGlnSerGlyGluAsnLeuProTyrLeuValAlaTyrGlnAlaThrValCysAla
 1022 ACAAAGCAGAGTGGGGAGAACCTTCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCT
 TGTTTCGTCTACCCCTCTTGGGAAGGAATGGACCATCGCATGGTTCGGTGGCACACGCGA
 1069 DRA3,
 ArgAlaGlnAlaProProProSerTrpAspGlnMetTrpLysCysLeuIleArgLeuLys
 1082 AGGGCTCAAGCCCCCTCCCCATCGTGGGACCAGATGTGGAAGTGTGTTGATTCGCCTCAAG

FIGURE 22 - Page 3

TCCCGAGTTCGGGGAGGGGGTAGCACCTGGTCTACACCTTCACAACTAAGCGGAGTTC

ProThrLeuHisGlyProThrProLeuLeuTyrArgLeuGlyAlaValGlnAsnGluIle
 1142 CCCACCCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTTCTAGAATGAAATC
 GGGTGGGAGGTACCCGGTTGTGGGGACGATATGTCTGACCCGCGACAAGTCTTACTTTAG
 ^
 1150 NCOI,

ThrLeuThrHisProValThrLysTyrIleMetThrCysMetSerAlaAspLeuGluVal
 1202 ACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATGTCGGCCGACCTGGAGGTC
 TGGGACTGCGTGGGTGAGTGGTTTATGTAGTACTGTACGTACAGCCGGCTGGACCTCCAG
 ^ ^ ^ ^ ^
 1230 BSPH1, 1234 DRD1, 1237 AVA3, 1245 EAG1 XMA3, 1250 DRD1,

ValThrSerThrTrpValLeuValGlyGlyValLeuAlaAlaLeuAlaAlaTyrCysLeu
 1262 GTCACGAGCAGCTGGGTGCTCGTTGGCGGCGTCTGGCTGCTTTGGCCGCGTATTGCCTG
 CAGTGCTCGTGGACCCACGAGCAACCGCCGAGGACCGACGAAACCGGCGCATAACGGAC

SerThrGlyCysValValIleValGlyArgValValLeuSerGlyLysProAlaIleIle
 1322 TCAACAGGCTGCGTGGTCATAGTGGGCAGGGTCGTCTTGTCGGGAAGCCGGCAATCATA
 AGTTGTCCGACGCACCAAGTATCACCCGTCCAGCAGAACAGGCCCTTCGGCCGTTAGTAT
 ^
 1369 NAEI,

ProAspArgGluValLeuTyrArgGluPheAspGluMetGluGluCysSerGlnHisLeu
 1382 CCTGACAGGGAAGTCTCTACCGAGAGTTCGATGAGATGGAAGAGTGTCTCTCAGCACTTA
 GGACTGTCCCTTCAGGAGATGGCTCTCAAGCTACTCTACCTTCTCAGGAGTCTGTAAT
 ^
 1385 DRD1,

ProTyrIleGluGlnGlyMetMetLeuAlaGluGlnPheLysGlnLysAlaLeuGlyLeu
 1442 CCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAGCAGAAAGGCCCTCGGCCTC
 GGCATGTAGCTCGTTCCTACTACGAGCGGCTCGTCAAGTTCGTCTTCGGGAGCCGGAG

LeuGlnThrAlaSerArgGlnAlaGluValIleAlaProAlaValGlnThrAsnTrpGln
 1502 CTGCAGACCGCTCCCGTCAGGCAGAGGTATCGCCCTGCTGTCCAGACCACTGGCAA
 GACGTCTGGCGCAGGGCAGTCCGTCTCCAATAGCGGGGACGACAGGTCTGGTTGACCGTT
 ^ ^
 1502 PSTI, 1507 TTH3I,

LysLeuGluThrPheTrpAlaLysHisMetTrpAsnPheIleSerGlyIleGlnTyrLeu
 1562 AAACGAGACCTTCTGGGCGAAGCATATGTGGAATTCATCAGTGGGATACAATACTTG
 TTTGAGCTCTGGAAGACCCGCTTCGTATACACCTGAAGTAGTCACCTATGTTATGAAC
 ^ ^
 1565 XHOI, 1586 NDEI,

AlaGlyLeuSerThrLeuProGlyAsnProAlaIleAlaSerLeuMetAlaPheThrAla
 1622 GCGGGCTTGTAACGCTGCCTGGTAACCCCGCCATTGCTTCATTGATGGCTTTTACAGCT
 CGCCCGAACAGTTGCGACGGACATTGGGGCGGTAACTAAGTAACACCGAAATGTCGA
 ^
 1643 BSTE2, 1677 ALWN1 PVU2,

AlaValThrSerProLeuThrThrSerGlnThrLeuLeuPheAsnIleLeuGlyGlyTrp
 1682 GCTGTACACAGCCCACTAACCCTAGCCAAACCTCCTCTCAACATATTGGGGGGGTGG
 CGACAGTGGTGGGTGATTGGTGATCGGTTTGGGAGGAGAAGTTGTATAACCCCCCACC

FIGURE 22 - Page 4

ValAlaAlaGlnLeuAlaAlaProGlyAlaAlaThrAlaPheValGlyAlaGlyLeuAla
 1742 GTGGCTGCCAGCTCGCCGCCCCGGTGCCGCTACTGCCTTTGTGGGCGCTGGCTTAGCT
 CACCGACGGGTGAGCGGGGGGCCACGGCGATGACGGAACACCCGCGACCGAATCGA
 ^
 1794 ESP1,
 GlyAlaAlaIleGlySerValGlyLeuGlyLysValLeuIleAspIleLeuAlaGlyTyr
 1802 GGGCGCGCCATCGGCAGTGTGGACTGGGGAAGGTCTCATAGACATCCTTGCGAGGTAT
 CCGCGGGCGGTAGCCGTCACAACTGACCCCTTCCAGGAGTATCTGTAGGAACGTCCCAT
 ^
 1802 KAS1 NARI,
 GlyAlaGlyValAlaGlyAlaLeuValAlaPheLysIleMetSerGlyGluValProSer
 1862 GGGCGGGGCGTGGCGGGAGCTCTTGTGGCATTCAAGATCATGAGCGGTGAGGTCCCTCC
 CCGCGCCCGCACCGCCCTCGAGAACACCGTAAGTTCTAGTACTCGCCACTCCAGGGGAGG
 ^
 1878 SACI, 1899 BSPH1,
 ThrGluAspLeuValAsnLeuLeuProAlaIleLeuSerProGlyAlaLeuValValGly
 1922 ACGGAGGACCTGGTCAATCTACTGCCCGCCATCCTCTCGCCCGAGCCCTCGTAGTCGGC
 TGCTCTGGACCAGTTAGATGACGGGCGGTAGGAGAGCGGGCCTCGGGAGCATCAGCCG
 ^
 1928 TTH3I,
 ValValCysAlaAlaIleLeuArgArgHisValGlyProGlyGluGlyAlaValGlnTrp
 1982 GTGGTCTGTGAGCAATACTGCGCCGGCACGTTGGCCCGGGCGAGGGGGCAGTGCACTGG
 CACCAGACACGTCGTTATGACGCGGGCGTGCAACCGGGCCCGCTCCCCCGTCACGTCACC
 ^
 2004 NAEI, 2017 SMAI XMAI,
 MetAsnArgLeuIleAlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal
 2042 ATGAACCGGCTGATAGCCTTCGCCTCCCGGGGAACCATGTTCCCCACGCACTACGTG
 TACTTGGCCGACTATCGGAAGCGGAGGGCCCCCTTGGTACAAAGGGGTGCGTGATGCAC
 ^
 2067 SMAI XMAI, 2093 DRA3,
 ProGluSerAspAlaAlaAlaArgValThrAlaIleLeuSerSerLeuThrValThrGln
 2102 CCGGAGAGCGATGCACTGCCCCGCGTCACTGCCATACTCAGCAGCCTCACTGTAACCCAG
 GGCCTCTCGCTACGTCGACGGGCGCAGTGACGGTATGAGTCGTGAGGTGACATTGGGTC
 ^
 2115 PVU2, 2159 ALWN1,
 LeuLeuArgArgLeuHisGlnTrpIleSerSerGluCysThrThrProCysSerGlySer
 2162 CTCTGAGGCGACTGCACCACTGGATAAGCTCGGAGTGTACCACTCCATGCTCCGGTTCC
 GAGGACTCCGCTGACGTGGTCACCTATTGAGCCTCACATGGTGAGGTACGAGGCCAAGG
 ^
 2164 MST2, 2220 ECON1,
 TrpLeuArgAspIleTrpAspTrpIleCysGluValLeuSerAspPheLysThrTrpLeu
 2222 TGGCTAAGGGACATCTGGGACTGGATATGCGAGGTGTTGAGCGACTTTAAGACCTGGCTA
 ACCGATTCCCTGTAGACCCTGACCTATACGCTCCACAACCTCGCTGAAATTCTGGACCGAT
 ^
 LysAlaLysLeuMetProGlnLeuProGlyIleProPheValSerCysGlnArgGlyTyr
 2282 AAAGCTAAGCTCATGCCACAGCTGCCTGGGATCCCCTTTGTGCTCTGCCAGCGCGGGTAT
 TTTGATTCGAGTACGGTGTGACGGACCTAGGGGAAACACAGGACGGTCGCGCCCAT
 ^
 2285 ESP1, 2300 PVU2, 2310 BAMHI,

FIGURE 22 - Page 5

2342 LysGlyValTrpArgGlyAspGlyIleMetHisThrArgCysHisCysGlyAlaGluIle
 AAGGGGGTCTGGCGAGGGGACGGCATCATGCACACTCGCTGCCACTGTGGAGCTGAGATC
 TTCCCCCAGACCGCTCCCTGCGGTAGTACGTGTGAGCGACGGTGACACCTCGACTCTAG

 2402 ThrGlyHisValLysAsnGlyThrMetArgIleValGlyProArgThrCysArgAsnMet
 ACTGGACATGTCAAAAACGGGACGATGAGGATCGTCGGTCCTAGGACCTGCAGGAACATG
 TGACCTGTACAGTTTTTGCCCTGCTACTCCTAGCAGCCAGGATCCTGGACGTCTTGTAC
 ^ ^ ^
 2425 BSAB1, 2441 AVR2, 2448 SSE83871, 2449 PSTI,

 2462 TrpSerGlyThrPheProIleAsnAlaTyrThrThrGlyProCysThrProLeuProAla
 TGGAGTGGGACCTTCCCCATTAATGCCTACACCACGGGCCCCCTGTACCCCCCTTCTCGCG
 ACCTCACCTGGAAGGGGTAATTACGGATGTGGTGCCCGGGACATGGGGGGAAGGACGC
 ^ ^
 2480 ASE1, 2497 APAI,

 2522 ProAsnTyrThrPheAlaLeuTrpArgValSerAlaGluGluTyrValGluIleArgGln
 CCGAACTACACGTTTCGCGCTATGGAGGGTGTCTGCAGAGGAATACGTGGAGATAAGGCAG
 GGCTTGATGTGCAAGCGCGATACCTCCCACAGACGTCTCCTTATGCACCTCTATTCCGTC
 ^
 2553 PSTI,

 2582 ValGlyAspPheHisTyrValThrGlyMetThrThrAspAsnLeuLysCysProCysGln
 GTGGGGGACTTCCACTACGTGACGGGTATGACTACTGACAATCTTAAATGCCCCGTGCCAG
 CCCCCCTGAAGGTGATGCACTGCCCATACTGATGACTGTTAGAATTTACGGGCACGGTC
 ^
 2594 DRA3,

 2642 ValProSerProGluPhePheThrGluLeuAspGlyValArgLeuHisArgPheAlaPro
 GTCCCATCGCCGAATTTTTACAGAATTGGACGGGGTGCGCCTACATAGGTTTGCGCCC
 CAGGGTAGCGGGCTTAAAAGTGTCTTAACCTGCCCCACGCGGATGTATCAAACGCGGG

 2702 ProCysLysProLeuLeuArgGluGluValSerPheArgValGlyLeuHisGluTyrPro
 CCCTGCAAGCCCTTGCTGCGGGAGGAGGTATCATTCAGAGTAGGACTCCACGAATACCCG
 GGGACGTTGCGGAACGACGCCCTCCTCCATAGTAAGTCTCATCTGAGGTGCTTATGGGC
 ^
 2757 HGIE2,

 2762 ValGlySerGlnLeuProCysGluProGluProAspValAlaValLeuThrSerMetLeu
 GTAGGGTCGCAATTACCTTGCGAGCCCGAACCGGACGTGGCCGTGTTGACGTCCATGCTC
 CATCCAGCGTTAATGGAACGCTCGGGCTTGGCCTGCACCGGCACAACCTGCAGGTACGAG
 ^
 2809 AAT2,

 2822 ThrAspProSerHisIleThrAlaGluAlaAlaGlyArgArgLeuAlaArgGlySerPro
 ACTGATCCCTCCCATATAACAGCAGAGGCGCGCGGCGAAGGTTGGCGAGGGGATCACCC
 TGAAGTAGGGAGGGTATATTGTCGTCTCCGCGGCGCGCTTCCAACCGCTCCCTAGTGGG
 ^
 2850 EAG1 XMA3,

 2882 ProSerValAlaSerSerSerAlaSerGlnLeuSerAlaProSerLeuLysAlaThrCys
 CCCTCTGTGGCCAGCTCCTCGGCTAGCCAGCTATCCGCTCCATCTCTCAAGGCAACTTGC
 GGGAGACACCGGTGAGGAGCCGATCGGTGATAGGCGAGGTAGAGAGTTCGGTTGAACG
 ^ ^
 2889 BALI, 2903 NHEI,

FIGURE 22 - Page 6

ThrAlaAsnHisAspSerProAspAlaGluLeuIleGluAlaAsnLeuLeuTrpArgGln
 2942 ACCGCTAACCATGACTCCCCTGATGCTGAGCTCATAGAGGCCAACCTCCTATGGAGGCAG
 TGGCGATTGGTACTGAGGGGACTACGACTCGAGTATCTCCGGTTGGAGGATACCTCCGTC
 ^ ^
 2966 ESP1, 2969 SACI,
 GluMetGlyGlyAsnIleThrArgValGluSerGluAsnLysValValIleLeuAspSer
 3002 GAGATGGGCGGCAACATCACCAGGGTTGAGTCAGAAAACAAAGTGGTGATTCTGGACTCC
 CTCTACCCGCCGTTGTAGTGGTCCCAACTCAGTCTTTTGTTCACCACTAAGACCTGAGG
 PheAspProLeuValAlaGluGluAspGluArgGluIleSerValProAlaGluIleLeu
 3062 TTCGATCCGCTTGTGGCGGAGGAGGACGAGCGGGAGATCTCCGTACCCGCAGAAATCCTG
 AAGCTAGGCGAACACCGCCTCCTCCTGCTCGCCCTCTAGAGGCATGGGCGTCTTTAGGAC
 ^
 3096 BGL2,
 ArgLysSerArgArgPheAlaGlnAlaLeuProValTrpAlaArgProAspTyrAsnPro
 3122 CGGAAGTCTCGGAGATTGCCCCAGGCCCTGCCCGTTTGGGCGCGGCGGACTATAACCCC
 GCCTTCAGAGCCTCTAAGCGGGTCCGGGACGGGCAAACCCGCGCCGCTGATATTGGGG
 ^
 3143 ALWN1, 3164 EAG1 XMA3,
 ProLeuValGluThrTrpLysLysProAspTyrGluProProValValHisGlyCysPro
 3182 CCGCTAGTGGAGACGTGAAAAAGCCGACTACGAACACCTGTGGTCCATGGCTGCCCCG
 GGCGATCACCTCTGCACCTTTTTCGGGCTGATGCTTGGTGGACACCAAGTACCGACGGGC
 ^
 3217 HGIE2, 3229 NCOI,
 LeuProProProLysSerProProValProProProArgLysLysArgThrValValLeu
 3242 CTTCCACCTCCAAAGTCCCTCCTGTGCCTCCGCCTCGGAAGAAGCGGACGGTGGTCTC
 GAAGGTGGAGGTTTCAGGGGAGGACACGGAGGCGGAGCCTTCTTCGCCTGCCACCAGGAG
 ThrGluSerThrLeuSerThrAlaLeuAlaGluLeuAlaThrArgSerPheGlySerSer
 3302 ACTGAATCAACCCTATCTACTGCCTTGGCCGAGCTCGCCACCAGAAGCTTTGGCAGCTCC
 TGACTTAGTTGGGATAGATGACGGAACCGGCTCGAGCGGTGGTCTTCGAAACCGTCGAGG
 ^ ^
 3332 SACI, 3346 HIND3,
 SerThrSerGlyIleThrGlyAspAsnThrThrThrSerSerGluProAlaProSerGly
 3362 TCAACTTCCGGCATTACGGGCGACAATACGACAACATCCTCTGAGCCCGCCCTTCTGGC
 AGTTGAAGGCCGTAATGCCCGCTGTTATGCTGTTGTAGGAGACTCGGGCGGGGAAGACCG
 CysProProAspSerAspAlaGluSerTyrSerSerMetProProLeuGluGlyGluPro
 3422 TGCCCCCCCCGACTCCGACGCTGAGTCTATTCTCCATGCCCCCCTGGAGGGGGAGCCT
 ACGGGGGGGCTGAGGCTGCGACTCAGGATAAGGAGGTACGGGGGGGACCTCCCCCTCGGA
 ^
 3437 EAM11051,
 GlyAspProAspLeuSerAspGlySerTrpSerThrValSerSerGluAlaAsnAlaGlu
 3482 GGGGATCCGGATCTTAGCGACGGGTCAATGGTCAACGGTCAGTAGTGAGGCCAACCGGGAG
 CCCCTAGGCCTAGAATCGCTGCCAGTACCAGTTGCCAGTCATCACTCCGGTTGCGCCTC
 ^ ^ ^
 3484 BAMHI, 3485 BSAB1, 3487 BSPE1,
 AspValValCysCysSerMetSerTyrSerTrpThrGlyAlaLeuValThrProCysAla
 3542 GATGTCGTGTGCTCAATGTCTTACTCTTGACAGGCGCACTCGTCAACCCGTGCGCC
 CTACAGCACACGACGAGTTACAGAATGAGAACCTGTCCCGTGAGCAGTGGGGCACGGC

FIGURE 22 - Page 7

3589 DRA3, 3600 SAC2,

AlaGluGluGlnLysLeuProIleAsnAlaLeuSerAsnSerLeuLeuArgHisHisAsn
 3602 GCGGAAGAACAGAACTGCCCATCAATGCACTAAGCAACTCGTTGCTACGTCACCACAAT
 CGCCTTCTTGCTTTGACGGGTAGTTACGTGATTCTGTTGAGCAACGATGCAGTGGTGTTA

3611 ALWN1, 3655 PFLM1,

LeuValTyrSerThrThrSerArgSerAlaCysGlnArgGlnLysLysValThrPheAsp
 3662 TTGGTGTATTCCACCACCTCACGCAGTGCTTGCCAAAGGCAGAAGAAAGTCACATTTGAC
 AACCACATAAGGTGGTGGAGTGCGTCACGAACGGTTTCCGTCTTCTTTCAGTGTAAGT

3681 DRA3,

ArgLeuGlnValLeuAspSerHisTyrGlnAspValLeuLysGluValLysAlaAlaAla
 3722 AGACTGCAAGTTCTGGACAGCCATTACCAGGACGTACTCAAGGAGGTTAAAGCAGCGCGC
 TCTGACGTTCAAGACCTGTCGGTAATGGTCTGTCATGAGTTCCTCCAATTCGTCGCGCGC

SerLysValLysAlaAsnLeuLeuSerValGluGluAlaCysSerLeuThrProProHis
 3782 TCAAAAGTGAAGGCTAACTTGCTATCCGTAGAGGAAGCTTGACGCCTGACGCCCCACAC
 AGTTTTCACTTCCGATTGAACGATAGGCATCTCCTTCGAACGTCGGACTGCGGGGGTGTG

3816 HIND3,

SerAlaLysSerLysPheGlyTyrGlyAlaLysAspValArgCysHisAlaArgLysAla
 3842 TCAGCCAAATCCAAGTTTGGTTATGGGGCAAAAGACGTCCGTTGCCATGCCAGAAAGGCC
 AGTCGGTTTAGGTTCAAACCAATACCCCGTTTTCTGCAGGCAACGGTACGGTCTTTCCGG

3875 AAT2, 3890 BGLI,

ValThrHisIleAsnSerValTrpLysAspLeuLeuGluAspAsnValThrProIleAsp
 3902 GTAACCCACATCAACTCCGTGTGGAAAGACCTTCTGGAAGACAATGTAACACCAATAGAC
 CATTGGGTGTAGTTGAGGCACACCTTCTGGAAGACCTTCTGTTACATTGTGGTTATCTG

ThrThrIleMetAlaLysAsnGluValPheCysValGlnProGluLysGlyGlyArgLys
 3962 ACTACCATCATGGCTAAGAACGAGTTTTCTGCGTTCAGCCTGAGAAGGGGGGTCGTAAG
 TGATGGTAGTACCGATTCTTGCTCCAAAAGACGCAAGTCGGACTCTTCCCCCAGCATTC

ProAlaArgLeuIleValPheProAspLeuGlyValArgValCysGluLysMetAlaLeu
 4022 CCAGCTCGTCTCATCGTGTCCCCGATCTGGGCGTGCGCGTGTGCGAAAAGATGGCTTTG
 GGTCGAGCAGAGTAGCACAAGGGGCTAGACCCGCACGCGCACACGCTTTTCTACCGAAAC

TyrAspValValThrLysLeuProLeuAlaValMetGlySerSerTyrGlyPheGlnTyr
 4082 TACGACGTGGTTACAAAGCTCCCCCTGGCCGTGATGGGAAGCTCCTACGGATTCCAATAC
 ATGCTGCACCAATGTTTCGAGGGGAACCGGCACTACCCTTCGAGGATGCCTAAGGTTATG

SerProGlyGlnArgValGluPheLeuValGlnAlaTrpLysSerLysLysThrProMet
 4142 TCACCAGGACAGCGGGTTGAATTCCTCGTGCAAGCGTGAAGTCCAAGAAAACCCCAATG
 AGTGGTCTGTGCCCCAACTTAAGGAGCACGTTTCGCACCTTCAGGTTCTTTTGGGGTTAC

4160 ECOR1,

GlyPheSerTyrAspThrArgCysPheAspSerThrValThrGluSerAspIleArgThr
 4202 GGGTCTCGTATGATACCCGCTGCTTTGACTCCACAGTCACTGAGAGCGACATCCGTACG
 CCCAAGAGCATACTATGGGCGACGAACTGAGGTGTCAGTGACTCTCGCTGTAGGCATGC

FIGURE 22 - Page 8

4229 DRD1, 4236 ALWN1,

4262 GluGluAlaIleTyrGlnCysCysAspLeuAspProGlnAlaArgValAlaIleLysSer
 GAGGAGGCAATCTACCAATGTTGTGACCTCGACCCCAAGCCGCGTGGCCATCAAGTCC
 CTCCTCCGTTAGATGGTTACAACACTGGAGCTGGGGGTTTCGGGCGCACCGGTAGTTCAGG

4301 BGLI, 4308 BALI,

4322 LeuThrGluArgLeuTyrValGlyGlyProLeuThrAsnSerArgGlyGluAsnCysGly
 CTCACCGAGAGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAACTGCGGC
 GAGTGGCTCTCCGAAATACAACCCCGGAGAATGGTTAAGTCCCCCTCTTGACGCCG

4345 APAI,

4382 TyrArgArgCysArgAlaSerGlyValLeuThrThrSerCysGlyAsnThrLeuThrCys
 TATCGCAGGTGCCGCGCAGCGGCGTACTGACAACCTAGCTGTGGTAACACCCCTCACTTGC
 ATAGCGTCCACGGCGCGCTCGCCGCATGACTGTTGATCGACACCATTGTGGGAGTGAACG

4442 TyrIleLysAlaArgAlaAlaCysArgAlaAlaGlyLeuGlnAspCysThrMetLeuVal
 TACATCAAGGCCCGGGCAGCCTGTCTGAGCCGCGAGGGCTCCAGGACTGCACCATGCTCGTG
 ATGTAGTTCCGGGCGCGTCCGGACAGCTCGGCGTCCCGAGGTCCTGACGTGGTACGAGCAC

4452 SMAI XMAI,

4502 CysGlyAspAspLeuValValIleCysGluSerAlaGlyValGlnGluAspAlaAlaSer
 TGTGGCGACGACTTAGTCGTTATCTGTGAAAGCGCGGGGTCCAGGAGGACGCGCGCAGC
 ACACCGCTGCTGAATCAGCAATAGACACTTTCGCGCCCCCAGGTCTCTCGCGCCGCTCG

4508 DRD1, 4511 TTH3I,

4562 LeuArgAlaPheThrGluAlaMetThrArgTyrSerAlaProProGlyAspProProGln
 CTGAGAGCCTTCACGGAGGCTATGACCAGGTACTCCGCCCCCCTGGGGACCCCCACAA
 GACTCTCGGAAGTGCTCCGATACTGGTCCATGAGGCGGGGGGACCCCTGGGGGTGTT

4622 ProGluTyrAspLeuGluLeuIleThrSerCysSerSerAsnValSerValAlaHisAsp
 CCAGAATACGACTTGGAGCTCATAACATCATGCTCCTCCAACGTGTCAGTCGCCCCACGAC
 GGTCTTATGCTGAACCTCGAGTATTGTAGTACGAGGAGGTTGCACAGTCAGCGGTGCTG

4637 SACI,

4682 GlyAlaGlyLysArgValTyrTyrLeuThrArgAspProThrThrProLeuAlaArgAla
 GCGCTGGAAAGAGGGTCTACTACCTACCCGTGACCCTACAACCCCCCTCGCGAGAGCT
 CCGCGACCTTCTCCCAGATGATGGAGTGGGCACTGGGATGTTGGGGGAGCGCTCTCGA

4731 NRUI,

4742 AlaTrpGluThrAlaArgHisThrProValAsnSerTrpLeuGlyAsnIleIleMetPhe
 GCGTGGGAGACAGCAAGACACACTCCAGTCAATTCCTGGCTAGGCAACATAATCATGTTT
 CGCACCTCTGTCGTTCTGTGTGAGGTGAGTTAAGGACCGATCCGTTGTATTAGTACAA

4802 AlaProThrLeuTrpAlaArgMetIleLeuMetThrHisPhePheSerValLeuIleAla
 GCCCCACACTGTGGGCGAGGATGATACTGATGACCCATTCTTTAGCGTCTTATAGCC
 CGGGGTGTGACACCCGCTCCTACTATGACTACTGGGTAAAGAAATCGCAGGAATATCGG

4806 PFLM1, 4807 DRA3,

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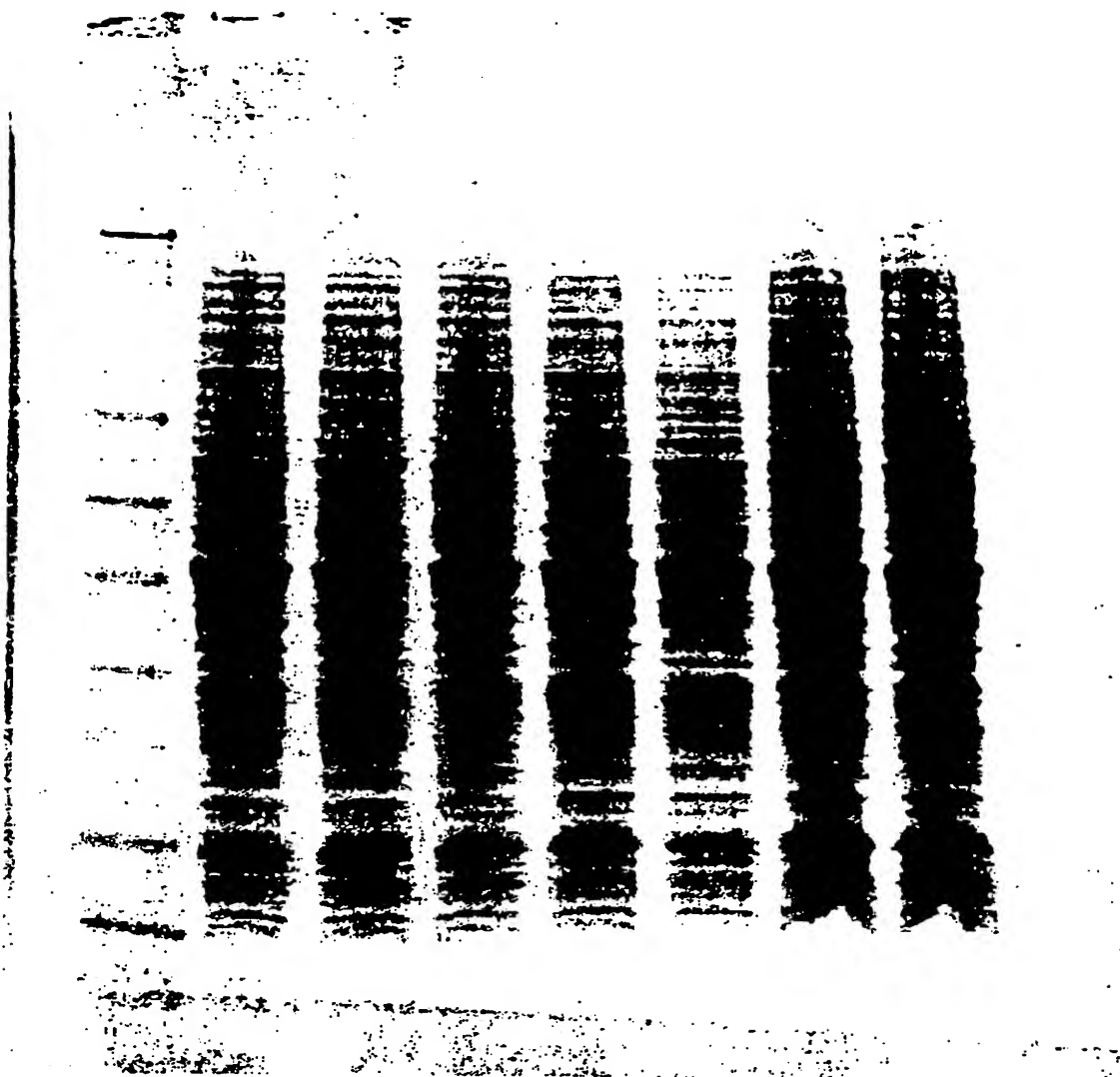
FIGURE 22 - Page 9

4862 AGGGACCAGCTTGAACAGGCCCTCGATTGCGAGATCTACGGGGCCTGCTACTCCATAGAA
 TCCCTGGTCGAACTTGTCCGGGAGCTAACGCTCTAGATGCCCCGACGATGAGGTATCTT
 4893 BGL2,
 ProLeuAspLeuProProIleIleGlnArgLeuHisGlyLeuSerAlaPheSerLeuHis
 4922 CCACTGGATCTACCTCCAATCATTCAAAGACTCCATGGCCTCAGCGCATTTTCACTCCAC
 GGTGACCTAGATGGAGGTTAGTAAGTTTCTGAGGTACCGGAGTCGCGTAAAAGTGAGGTG
 4954 NCOI,
 SerTyrSerProGlyGluIleAsnArgValAlaAlaCysLeuArgLysLeuGlyValPro
 4982 AGTTACTCTCCAGGTGAAATCAATAGGGTGGCCGCATGCCTCAGAAAACCTTGGGGTACCG
 TCAATGAGAGGTCCACTTTAGTTATCCACCGGCGTACGGAGTCTTTTGAACCCCATGGC
 5015 SPHI, 5035 KPN1,
 ProLeuArgAlaTrpArgHisArgAlaArgSerValArgAlaArgLeuLeuAlaArgGly
 5042 CCCTTGCGAGCTTGGAGACACCGGGCCCGGAGCGTCCGCGCTAGGCTTCTGGCCAGAGGA
 GGGAACGCTCGAACCTCTGTGGCCCGGCGCTCGCAGGCGCGATCCGAAGACCGGTCTCCT
 5064 APAI, 5091 BALI,
 GlyArgAlaAlaIleCysGlyLysTyrLeuPheAsnTrpAlaValArgThrLysLeuLys
 5102 GGCAGGGCTGCCATATGTGGCAAGTACCTCTTCAACTGGGCAGTAAGAACAAAGCTCAAA
 CCGTCCCACGCTATACACCGTTCATGGAGAAGTTGACCCGTCATTCTTGTTCGAGTTT
 5113 NDEI,
 LeuThrProIleAlaAlaAlaGlyGlnLeuAspLeuSerGlyTrpPheThrAlaGlyTyr
 5162 CTCACTCCAATAGCGGCCGCTGGCCAGCTGGACTTGTCCGGCTGGTTCACGGCTGGCTAC
 GAGTGAGGTTATCGCCGGCGACCGGTGACCTGAACAGGCCGACCAAGTGCCGACCGATG
 5174 NOTI, 5175 EAG1 XMA3, 5182 BALI, 5186 PVU2,
 SerGlyGlyAspIleTyrHisSerValSerHisAlaArgProArgTrpIleTrpPheCys
 5222 AGCGGGGGGAGACATTTATCACAGCGTGTCTCATGCCCCGGCCCCGCTGGATCTGGTTTGC
 TCGCCCCCTCTGTAAATAGTGTGCGACAGAGTACGGGCCGGGGCGACCTAGACCAAAACG
 5240 DRA3,
 LeuLeuLeuLeuAlaAlaGlyValGlyIleTyrLeuLeuProAsnArgMetSerThrAsn
 5282 CTACTCCTGCTTGCTGCGAGGGTAGGCATCTACCTCCTCCCCAACCGAATGAGCAGCAAT
 GATGAGGACGAACGACGTCCCATCCGTAGATGGAGGAGGGTTGGCTTACTCGTGCTTA
 5295 PSTI,
 ProLysProGlnArgLysThrLysArgAsnThrAsnArgArgProGlnAspValLysPhe
 5342 CCTAAACCTCAAAGAAAGACCAACGTAACACCAACCGGGCGCCGAGGACGTCAAGTTC
 GGATTTGGAGTTTCTTTCTGGTTTGCATTGTGGTTGGCCGCGCGTCTGCAGTTCAAG
 5380 NOTI, 5381 EAG1 XMA3, 5390 AAT2, 5401 SMAI XMAI,
 ProGlyGlyGlyGlnIleValGlyGlyValTyrLeuLeuProArgArgGlyProArgLeu
 5402 CCGGGTGGCGGTCAGATCGTTGGTGGAGTTTACTTGTGTCGCGCAGGGGCCCTAGATTG
 GGCCACCGCCAGTCTAGCAACCACCTCAAATGAACAACGGCGCGTCCCCGGGATCAAC

FIGURE 22 - Page 10

5449 APAI,
GlyValArgAlaThrArgLysThrSerGluArgSerGlnProArgGlyArgArgGlnPro
5462 GGTGTGCGCGCGACGAGAAAGACTTCCGAGCGGTCGCAACCTCGAGGTAGACGTCAGCCT
CCACACGCGCGCTGCTCTTTCTGAAGGCTCGCCAGCGTTGGAGCTCCATCTGCAGTCGGA
5467 BSSH2, 5478 XMNI, 5502 XHOI, 5511 AAT2,
IleProLysAlaArgArgProGluGlyArgThrTrpAlaGlnProGlyTyrProTrpPro
5522 ATCCCCAAGGCTCGTCGGCCCGAGGGCAGGACCTGGGCTCAGCCCGGGTACCCTTGGCCC
TAGGGGTTCCGAGCAGCCGGGCTCCCGTCTGGACCCGAGTCGGGCCCATGGGAACCGGG
5548 ALWN1, 5558 ESP1, 5564 SMAI XMAI, 5568 KPNI,
LeuTyrGlyAsnGluGlyCysGlyTrpAlaGlyTrpLeuLeuSerProArgGlySerArg
5582 CTCTATGGCAATGAGGGCTGCGGGTGGGCGGGATGGCTCCTGTCTCCCGTGGCTCTCGG
GAGATACCGTTACTCCCGACGCCCCACCCGCCCTACCGAGGACAGAGGGGCACCGAGAGCC
ProSerTrpGlyProThrAspProArgArgArgSerArgAsnLeuGlyLysValIleAsp
5642 CCTAGCTGGGGCCCCACAGACCCCGGCGTAGGTCGCGCAATTGGGTAAGGTCATCGAT
GGATCGACCCCGGGGTGTCTGGGGGCCGATCCAGCGCGTTAAACCCATTCCAGTAGCTA
5650 APAI, 5696 CLAI,
ThrLeuThrCysGlyPheAlaAspLeuMetGlyTyrIleProLeuValGlyAlaProLeu
5702 ACCCTTACGTGCGGCTTCGCCGACCTCATGGGGTACATACCGCTCGTCGGCGCCCCCTCTT
TGGGAATGCACGCCGAAGCGGCTGGAGTACCCCATGTATGGCGAGCAGCCGCGGGGAGAA
5724 HGIE2, 5750 KAS1 NARI, 5756 ECON1,
GlyGlyAlaAlaArgAlaOC AM
5762 GGAGGCGCTGCCAGGGCCTAATAGTCGAC
CCTCCGCGACGGTCCCGGATTATCAGCTG
5785 SALI,

FIGURE 23



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Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys
      65             70             75

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His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp
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| 400 405 410 | |
| gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc gtc ctg gct gct ttg | 3279 |
| Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu | |
| 415 420 425 430 | |
| gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc ata gtg ggc agg gtc | 3327 |
| Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val | |
| 435 440 445 | |
| gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa gtc ctc tac | 3375 |
| Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr | |
| 450 455 460 | |
| cga gag ttc gat gag atg gaa gag tgc tct cag cac tta ccg tac atc | 3423 |
| Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile | |
| 465 470 475 | |
| gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag gcc ctc ggc | 3471 |
| Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly | |
| 480 485 490 | |
| ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc cct gct gtc | 3519 |
| Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val | |
| 495 500 505 510 | |
| cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag cat atg tgg | 3567 |
| Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp | |
| 515 520 525 | |
| aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca acg ctg cct | 3615 |
| Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro | |
| 530 535 540 | |
| ggt aac ccc gcc att gct tca ttg atg gct ttt aca gct gct gtc acc | 3663 |
| Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr | |
| 545 550 555 | |
| agc cca cta acc act agc caa acc ctc ctc ttc aac ata ttg ggg ggg | 3711 |
| Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly | |
| 560 565 570 | |

| | |
|---|------|
| tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act gcc ttt gtg | 3759 |
| Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val | |
| 575 580 585 590 | |
| ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga ctg ggg aag | 3807 |
| Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys | |
| 595 600 605 | |
| gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg gcg gga gct | 3855 |
| Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala | |
| 610 615 620 | |
| ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc acg gag gac | 3903 |
| Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp | |
| 625 630 635 | |
| ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc ctc gta gtc | 3951 |
| Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val | |
| 640 645 650 | |
| ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc ccg ggc gag | 3999 |
| Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu | |
| 655 660 665 670 | |
| ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc tcc cgg ggg | 4047 |
| Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly | |
| 675 680 685 | |
| aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat gca gct gcc | 4095 |
| Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala | |
| 690 695 700 | |
| cgc gtc act gcc ata ctc agc agc ctc act gta acc cag ctc ctg agg | 4143 |
| Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg | |
| 705 710 715 | |
| cga ctg cac cag tgg ata agc tcg gag tgt acc act cca tgc tcc ggt | 4191 |
| Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly | |
| 720 725 730 | |
| tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg ttg agc gac | 4239 |
| Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp | |
| 735 740 745 750 | |
| ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg cct ggg atc | 4287 |
| Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile | |
| 755 760 765 | |
| ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg cga ggg gac | 4335 |
| Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp | |
| 770 775 780 | |
| ggc atc atg cac act cgc tgc cac tgt gga gct gag atc act gga cat | 4383 |
| Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His | |
| 785 790 795 | |
| gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc tgc agg aac | 4431 |
| Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn | |
| 800 805 810 | |

| | |
|---|------|
| atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg ggc ccc tgt | 4479 |
| Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys | |
| 815 820 825 830 | |
| acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg agg gtg tct | 4527 |
| Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser | |
| 835 840 845 | |
| gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc cac tac gtg | 4575 |
| Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val | |
| 850 855 860 | |
| acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag gtc cca tcg | 4623 |
| Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser | |
| 865 870 875 | |
| ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat agg ttt gcg | 4671 |
| Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala | |
| 880 885 890 | |
| ccc ccc tgc aag ccc ttg ctg cgg gag gag gta tca ttc aga gta gga | 4719 |
| Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly | |
| 895 900 905 910 | |
| ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag ccc gaa ccg | 4767 |
| Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro | |
| 915 920 925 | |
| gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc cat ata aca | 4815 |
| Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr | |
| 930 935 940 | |
| gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc ccc tct gtg | 4863 |
| Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val | |
| 945 950 955 | |
| gcc agc tcc tcg gct agc cag cta tcc gct cea tct ctc aag gca act | 4911 |
| Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr | |
| 960 965 970 | |
| tgc acc gct aac cat gac tcc cct gat gct gag ctc ata gag gcc aac | 4959 |
| Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn | |
| 975 980 985 990 | |
| ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg gtt gag tca | 5007 |
| Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser | |
| 995 1000 1005 | |
| gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt gtg gcg gag | 5055 |
| Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu | |
| 1010 1015 1020 | |
| gag gac gag ccg gag atc tcc gta ccc gca gaa atc ctg ccg aag tct | 5103 |
| Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu Arg Lys Ser | |
| 1025 1030 1035 | |
| cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg ccg ccg gac tat aac | 5151 |
| Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro Asp Tyr Asn | |
| 1040 1045 1050 | |

ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa cca cct gtg 5199
 Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val
 1055 1060 1065 1070

gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct gtg cct ccg 5247
 Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro
 1075 1080 1085

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 Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr Leu Ser Thr
 1090 1095 1100

gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc tca act tcc 5343
 Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser
 1105 1110 1115

ggc att acg ggc gac aat acg aca aca tcc tct gag ccc gcc cct tct 5391
 Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro Ala Pro Ser
 1120 1125 1130

ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc atg ccc ccc 5439
 Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro
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ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg tca tgg tca 5487
 Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser
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acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc tgc tca atg 5535
 Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys Cys Ser Met
 1170 1175 1180

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 Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu
 1185 1190 1195

cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta cgt cac cac 5631
 Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His
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 Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys
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aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat tac cag gac 5727
 Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp
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gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag gct aac ttg 5775
 Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu
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cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac tca gcc aaa 5823
 Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys
 1265 1270 1275

tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat gcc aga aag 5871
 Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys
 1280 1285 1290

| | |
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| gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg gaa gac aat | 5919 |
| Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn | |
| 1295 1300 1305 1310 | |
| gta aca cca ata gac act acc atc atg gct aag aac gag gtt ttc tgc | 5967 |
| Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys | |
| 1315 1320 1325 | |
| gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc atc gtg ttc | 6015 |
| Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe | |
| 1330 1335 1340 | |
| ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg tac gac gtg | 6063 |
| Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val | |
| 1345 1350 1355 | |
| gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac gga ttc caa | 6111 |
| Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln | |
| 1360 1365 1370 | |
| tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg tgg aag tcc | 6159 |
| Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser | |
| 1375 1380 1385 1390 | |
| aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc ttt gac tcc | 6207 |
| Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser | |
| 1395 1400 1405 | |
| aca gtc act gag agc gac atc cgt acg gag gag gca atc tac caa tgt | 6255 |
| Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys | |
| 1410 1415 1420 | |
| tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc ctc acc gag | 6303 |
| Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu | |
| 1425 1430 1435 | |
| agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg gag aac tgc | 6351 |
| Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys | |
| 1440 1445 1450 | |
| ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act agc tgt ggt | 6399 |
| Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly | |
| 1455 1460 1465 1470 | |
| aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt cga gcc gca | 6447 |
| Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala | |
| 1475 1480 1485 | |
| ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac tta gtc gtt | 6495 |
| Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val | |
| 1490 1495 1500 | |
| atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc ctg aga gcc | 6543 |
| Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala | |
| 1505 1510 1515 | |
| ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg gac ccc cca | 6591 |
| Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro | |
| 1520 1525 1530 | |

9

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<211> 1771

<212> PRT

<213> Hepatitis C virus

<220>

<223> Description of Artificial Sequence: Hepatitis C pns345

<400> 2

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Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His
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Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
100 105 110

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
115 120 125

Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
130 135 140

Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
145 150 155 160

Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala

12

Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
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 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
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 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
 515 520 525
 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn
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 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
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 Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val
 565 570 575
 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
 580 585 590
 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
 610 615 620
 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
 625 630 635 640
 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
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 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
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 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
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 740 745 750
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 770 775 780
 Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
 785 790 795 800

Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
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 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
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 965 970 975
 Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
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 Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn
 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
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 1170 1175 1180
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 Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu Leu Ser
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 Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys
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 Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn Val Thr
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Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr
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Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala
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| Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly | |
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| Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg Pro Ser Gly | |
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| Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro | |
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| Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys | |
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| Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala | |
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| | | | | | | | | | | | | | | | | |
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| Ser | Trp | Leu | Arg | Asp | Ile | Trp | Asp | Trp | Ile | Cys | Glu | Val | Leu | Ser | Asp | |
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| Pro | Phe | Val | Ser | Cys | Gln | Arg | Gly | Tyr | Lys | Gly | Val | Trp | Arg | Gly | Asp | |
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| Gly | Ile | Met | His | Thr | Arg | Cys | His | Cys | Gly | Ala | Glu | Ile | Thr | Gly | His | |
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| Val | Lys | Asn | Gly | Thr | Met | Arg | Ile | Val | Gly | Pro | Arg | Thr | Cys | Arg | Asn | |
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| Thr | Pro | Leu | Pro | Ala | Pro | Asn | Tyr | Thr | Phe | Ala | Leu | Trp | Arg | Val | Ser | |
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| 1075 1080 1085 | |
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| Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr Leu Ser Thr | |
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 Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp
 1235 1240 1245

gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag gct aac ttg 5775
 Val Leu Lys Glu Val Lys Ala Ala Ser Lys Val Lys Ala Asn Leu
 1250 1255 1260

cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac tca gcc aaa 5823
 Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys
 1265 1270 1275

tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat gcc aga aag 5871
 Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys
 1280 1285 1290

gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg gaa gac aat 5919
 Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn
 1295 1300 1305 1310

gta aca cca ata gac act acc atc atg gct aag aac gag gtt ttc tgc 5967
 Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys
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gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc atc gtg ttc 6015
 Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe
 1330 1335 1340

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| ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg tac gac gtg Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val 1345 1350 1355 | 6063 |
| gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac gga ttc caa Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln 1360 1365 1370 | 6111 |
| tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg tgg aag tcc Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser 1375 1380 1385 1390 | 6159 |
| aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc ttt gac tcc Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser 1395 1400 1405 | 6207 |
| aca gtc act gag agc gac atc cgt acg gag gag gca atc tac caa tgt Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys 1410 1415 1420 | 6255 |
| tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc ctc acc gag Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu 1425 1430 1435 | 6303 |
| agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg gag aac tgc Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys 1440 1445 1450 | 6351 |
| ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act agc tgt ggt Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly 1455 1460 1465 1470 | 6399 |
| aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt cga gcc gca Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala 1475 1480 1485 | 6447 |
| ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac tta gtc gtt Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val 1490 1495 1500 | 6495 |
| atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc ctg aga gcc Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala 1505 1510 1515 | 6543 |
| ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg gac ccc cca Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro 1520 1525 1530 | 6591 |
| caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc tcc aac gtg Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val 1535 1540 1545 1550 | 6639 |
| tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac ctc acc cgt Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg 1555 1560 1565 | 6687 |
| gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca gca aga cac Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His 1570 1575 1580 | 6735 |

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 Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile
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 Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala
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tgc tac tcc ata gaa cca ctg gat cta cct cca atc att caa aga ctc 6927
 Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu
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 Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg
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 Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg
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Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
100 105 110

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
115 120 125

Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
130 135 140

Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
145 150 155 160

Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala
165 170 175

Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val
180 185 190

Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe
195 200 205

Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe
210 215 220

Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile Thr Leu Pro Gln Asp
225 230 235 240

Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr Gly Arg Gly Lys Pro

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|
| Gly | Ile | Tyr | Arg | Phe | Val | Ala | Pro | Gly | Glu | Arg | Pro | Ser | Gly | Met | Phe | | | | |
| | | | 260 | | | | | 265 | | | | | 270 | | | | | | |
| Asp | Ser | Ser | Val | Leu | Cys | Glu | Cys | Tyr | Asp | Ala | Gly | Cys | Ala | Trp | Tyr | | | | |
| | | 275 | | | | | 280 | | | | | 285 | | | | | | | |
| Glu | Leu | Thr | Pro | Ala | Glu | Thr | Thr | Val | Arg | Leu | Arg | Ala | Tyr | Met | Asn | | | | |
| | 290 | | | | | 295 | | | | | 300 | | | | | | | | |
| Thr | Pro | Gly | Leu | Pro | Val | Cys | Gln | Asp | His | Leu | Glu | Phe | Trp | Glu | Gly | | | | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | | | | |
| Val | Phe | Thr | Gly | Leu | Thr | His | Ile | Asp | Ala | His | Phe | Leu | Ser | Gln | Thr | | | | |
| | | | 325 | | | | | 330 | | | | | | 335 | | | | | |
| Lys | Gln | Ser | Gly | Glu | Asn | Leu | Pro | Tyr | Leu | Val | Ala | Tyr | Gln | Ala | Thr | | | | |
| | | | 340 | | | | | 345 | | | | | 350 | | | | | | |
| Val | Cys | Ala | Arg | Ala | Gln | Ala | Pro | Pro | Pro | Ser | Trp | Asp | Gln | Met | Trp | | | | |
| | | 355 | | | | | 360 | | | | | 365 | | | | | | | |
| Lys | Cys | Leu | Ile | Arg | Leu | Lys | Pro | Thr | Leu | His | Gly | Pro | Thr | Pro | Leu | | | | |
| | 370 | | | | | 375 | | | | | 380 | | | | | | | | |
| Leu | Tyr | Arg | Leu | Gly | Ala | Val | Gln | Asn | Glu | Ile | Thr | Leu | Thr | His | Pro | | | | |
| 385 | | | | 390 | | | | | | 395 | | | | | 400 | | | | |
| Val | Thr | Lys | Tyr | Ile | Met | Thr | Cys | Met | Ser | Ala | Asp | Leu | Glu | Val | Val | | | | |
| | | | 405 | | | | | 410 | | | | | | 415 | | | | | |
| Thr | Ser | Thr | Trp | Val | Leu | Val | Gly | Gly | Val | Leu | Ala | Ala | Leu | Ala | Ala | | | | |
| | | | 420 | | | | | 425 | | | | | 430 | | | | | | |
| Tyr | Cys | Leu | Ser | Thr | Gly | Cys | Val | Val | Ile | Val | Gly | Arg | Val | Val | Leu | | | | |
| | 435 | | | | | 440 | | | | | 445 | | | | | | | | |
| Ser | Gly | Lys | Pro | Ala | Ile | Ile | Pro | Asp | Arg | Glu | Val | Leu | Tyr | Arg | Glu | | | | |
| | 450 | | | | | 455 | | | | | 460 | | | | | | | | |
| Phe | Asp | Glu | Met | Glu | Glu | Cys | Ser | Gln | His | Leu | Pro | Tyr | Ile | Glu | Gln | | | | |
| 465 | | | | 470 | | | | | | 475 | | | | | 480 | | | | |
| Gly | Met | Met | Leu | Ala | Glu | Gln | Phe | Lys | Gln | Lys | Ala | Leu | Gly | Leu | Leu | | | | |
| | | | 485 | | | | | 490 | | | | | 495 | | | | | | |
| Gln | Thr | Ala | Ser | Arg | Gln | Ala | Glu | Val | Ile | Ala | Pro | Ala | Val | Gln | Thr | | | | |
| | | 500 | | | | | | 505 | | | | | 510 | | | | | | |
| Asn | Trp | Gln | Lys | Leu | Glu | Thr | Phe | Trp | Ala | Lys | His | Met | Trp | Asn | Phe | | | | |
| | | 515 | | | | | 520 | | | | | 525 | | | | | | | |
| Ile | Ser | Gly | Ile | Gln | Tyr | Leu | Ala | Gly | Leu | Ser | Thr | Leu | Pro | Gly | Asn | | | | |
| | 530 | | | | | 535 | | | | | 540 | | | | | | | | |
| Pro | Ala | Ile | Ala | Ser | Leu | Met | Ala | Phe | Thr | Ala | Ala | Val | Thr | Ser | Pro | | | | |
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Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val
 565 570 575
 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
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 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
 610 615 620
 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
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 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
 675 680 685
 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu
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 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735
 Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
 755 760 765
 Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile
 770 775 780
 Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
 785 790 795 800
 Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
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 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
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 835 840 845
 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
 850 855 860
 Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu
 865 870 875 880

Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro
 885 890 895
 Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
 900 905 910
 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
 Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu
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 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
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 965 970 975
 Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
 980 985 990
 Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn
 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
 1010 1015 1020
 Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Arg Arg
 025 1030 1035 1040
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 Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Pro Arg
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 1155 1160 1165
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Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu
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Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val
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Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro
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Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro
 1570 1575 1580

Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp
 585 1590 1595 1600

Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg
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Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr
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Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly
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Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg
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Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Ala Trp
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Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg Gly Gly
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Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Arg Thr
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Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly Gln Leu Asp Leu Ser
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Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Val
 1730 1735 1740

Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys Leu Leu Leu Leu Ala
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<212> DNA

<213> Artificial Sequence

<220>

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gccagcaaga cgtagcccag cgcgtcggcc gccatgccgg cgataatggc ctgcttctcg 11100
ccgaaacgtt tgggtggcggg accagtgacg aaggcttgag cgagggcggtg caagattccg 11160
aataccgcaa gcgacaggcc gatcatcgtc gcgctccagc gaaagcggtc ctgcgccgaa 11220
atgaccaga gcgctgccgg cacctgtcct acgagttgca tgataaagaa gacagtcata 11280
agtgcggcga cgatagtcac gcccgcgcc caccggaagg agctgactgg gttgaaggct 11340
ctcaagggca tcggctgagg atccttcaat atgcgcacat acgctgttat gttcaaggct 11400
ccttcgttta agaacgaaag cgttcttctt tttgagggat gtttcaagtt gttcaaatct 11460
atcaaatttg caaatcccca gtctgtatct agagcggttg atcgggtgat cgatttggtta 11520
attaaattga tgggtgtcacc attaccaggt ctgatatac caatggcaaa ctgagcacia 11580
caataccagt ccggatcaac tggcaccatc tctcccgtag tctcatctaa ttttcttcc 11640
ggatgagggt ccagatatac cgcaacacct ttattatggg ttcctgagg gaataataga 11700
atgtcccatt cgaaatcacc aattctaaac ctgggcgaat tgtatttcgg gtttggtaac 11760
tcgttccagt caggaatgtt ccacgtgaag ctatcttcca gcaaagtctc cacttcttca 11820

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|--|
| Leu | Ala | Thr | Ala | Thr | Pro | Pro | Gly | Ser | Val | Thr | Val | Pro | His | Pro | Asn | | |
| | | | | 110 | | | | | 115 | | | | | 120 | | | |
| atc | gag | gag | gtt | gct | ctg | tcc | acc | acc | gga | gag | atc | cct | ttt | tac | ggc | 13155 | |
| Ile | Glu | Glu | Val | Ala | Leu | Ser | Thr | Thr | Gly | Glu | Ile | Pro | Phe | Tyr | Gly | | |
| | | | 125 | | | | | 130 | | | | | 135 | | | | |
| aag | gct | atc | ccc | ctc | gaa | gta | atc | aag | ggg | ggg | aga | cat | ctc | atc | ttc | 13203 | |
| Lys | Ala | Ile | Pro | Leu | Glu | Val | Ile | Lys | Gly | Gly | Arg | His | Leu | Ile | Phe | | |
| | | | 140 | | | | | 145 | | | | 150 | | | | | |
| tgt | cat | tca | aag | aag | aag | tgc | gac | gaa | ctc | gcc | gca | aag | ctg | gtc | gca | 13251 | |
| Cys | His | Ser | Lys | Lys | Lys | Cys | Asp | Glu | Leu | Ala | Ala | Lys | Leu | Val | Ala | | |
| | | | 155 | | | | 160 | | | | | 165 | | | | | |
| ttg | ggc | atc | aat | gcc | gtg | gcc | tac | tac | cgc | ggg | ctt | gac | gtg | tcc | gtc | 13299 | |
| Leu | Gly | Ile | Asn | Ala | Val | Ala | Tyr | Tyr | Arg | Gly | Leu | Asp | Val | Ser | Val | | |
| | | | 170 | | | | 175 | | | | 180 | | | | 185 | | |
| atc | ccg | acc | agc | ggc | gat | gtt | gtc | gtc | gtg | gca | acc | gat | gcc | ctc | atg | 13347 | |
| Ile | Pro | Thr | Ser | Gly | Asp | Val | Val | Val | Val | Ala | Thr | Asp | Ala | Leu | Met | | |
| | | | | 190 | | | | | | 195 | | | | 200 | | | |
| acc | ggc | tat | acc | ggc | gac | ttc | gac | tcg | gtg | ata | gac | tgc | aat | acg | tgt | 13395 | |
| Thr | Gly | Tyr | Thr | Gly | Asp | Phe | Asp | Ser | Val | Ile | Asp | Cys | Asn | Thr | Cys | | |
| | | | 205 | | | | | 210 | | | | | 215 | | | | |
| gtc | acc | cag | aca | gtc | gat | ttc | agc | ctt | gac | cct | acc | ttc | acc | att | gag | 13443 | |
| Val | Thr | Gln | Thr | Val | Asp | Phe | Ser | Leu | Asp | Pro | Thr | Phe | Thr | Ile | Glu | | |
| | | | 220 | | | | | 225 | | | | | 230 | | | | |
| aca | atc | acg | ctc | ccc | caa | gat | gct | gtc | tcc | cgc | act | caa | cgt | cgg | ggc | 13491 | |
| Thr | Ile | Thr | Leu | Pro | Gln | Asp | Ala | Val | Ser | Arg | Thr | Gln | Arg | Arg | Gly | | |
| | | | 235 | | | | 240 | | | | 245 | | | | | | |
| agg | act | ggc | agg | ggg | aag | cca | ggc | atc | tac | aga | ttt | gtg | gca | ccg | ggg | 13539 | |
| Arg | Thr | Gly | Arg | Gly | Lys | Pro | Gly | Ile | Tyr | Arg | Phe | Val | Ala | Pro | Gly | | |
| | | | 250 | | | | 255 | | | | 260 | | | | 265 | | |
| gag | cgc | ccc | tcc | ggc | atg | ttc | gac | tcg | tcc | gtc | ctc | tgt | gag | tgc | tat | 13587 | |
| Glu | Arg | Pro | Ser | Gly | Met | Phe | Asp | Ser | Ser | Val | Leu | Cys | Glu | Cys | Tyr | | |
| | | | | 270 | | | | | | 275 | | | | | 280 | | |
| gac | gca | ggc | tgt | gct | tgg | tat | gag | ctc | acg | ccc | gcc | gag | act | aca | gtt | 13635 | |
| Asp | Ala | Gly | Cys | Ala | Trp | Tyr | Glu | Leu | Thr | Pro | Ala | Glu | Thr | Thr | Val | | |
| | | | 285 | | | | | 290 | | | | | 295 | | | | |
| agg | cta | cga | gcg | tac | atg | aac | acc | ccg | ggg | ctt | ccc | gtg | tgc | cag | gac | 13683 | |
| Arg | Leu | Arg | Ala | Tyr | Met | Asn | Thr | Pro | Gly | Leu | Pro | Val | Cys | Gln | Asp | | |
| | | | 300 | | | | | 305 | | | | 310 | | | | | |
| cat | ctt | gaa | ttt | tgg | gag | ggc | gtc | ttt | aca | ggc | ctc | act | cat | ata | gat | 13731 | |
| His | Leu | Glu | Phe | Trp | Glu | Gly | Val | Phe | Thr | Gly | Leu | Thr | His | Ile | Asp | | |
| | | | 315 | | | | 320 | | | | | 325 | | | | | |
| gcc | cac | ttt | cta | tcc | cag | aca | aag | cag | agt | ggg | gag | aac | ctt | cct | tac | 13779 | |
| Ala | His | Phe | Leu | Ser | Gln | Thr | Lys | Gln | Ser | Gly | Glu | Asn | Leu | Pro | Tyr | | |
| | | | 330 | | | | 335 | | | | 340 | | | | 345 | | |

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|---|-------|
| ctg gta gcg tac caa gcc acc gtg tgc gct agg gct caa gcc cct ccc | 13827 |
| Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro | |
| 350 355 360 | |
| cca tcg tgg gac cag atg tgg aag tgt ttg att cgc ctc aag ccc acc | 13875 |
| Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr | |
| 365 370 375 | |
| ctc cat ggg cca aca ccc ctg cta tac aga ctg ggc gct gtt cag aat | 13923 |
| Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn | |
| 380 385 390 | |
| gaa atc acc ctg acg cac cca gtc acc aaa tac atc atg aca tgc atg | 13971 |
| Glu Ile Thr Leu Thr His Pro Val Thr Lys Tyr Ile Met Thr Cys Met | |
| 395 400 405 | |
| tcg gcc gac ctg gag gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc | 14019 |
| Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly | |
| 410 415 420 425 | |
| gtc ctg gct gct ttg gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc | 14067 |
| Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val | |
| 430 435 440 | |
| ata gtg ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac | 14115 |
| Ile Val Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp | |
| 445 450 455 | |
| agg gaa gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag | 14163 |
| Arg Glu Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Cys Ser Gln | |
| 460 465 470 | |
| cac tta ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag | 14211 |
| His Leu Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys | |
| 475 480 485 | |
| cag aag gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt | 14259 |
| Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val | |
| 490 495 500 505 | |
| atc gcc cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg | 14307 |
| Ile Ala Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp | |
| 510 515 520 | |
| gcg aag cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc | 14355 |
| Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly | |
| 525 530 535 | |
| ttg tca acg ctg cct ggt aac ccc gcc att gct tca ttg atg gct ttt | 14403 |
| Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe | |
| 540 545 550 | |
| aca gct gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc | 14451 |
| Thr Ala Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe | |
| 555 560 565 | |
| aac ata ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc | 14499 |
| Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala | |
| 570 575 580 585 | |

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|---|-------|
| gct act gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt | 14547 |
| Ala Thr Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser | |
| 590 595 600 | |
| gtt gga ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg | 14595 |
| Val Gly Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala | |
| 605 610 615 | |
| ggc gtg gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc | 14643 |
| Gly Val Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val | |
| 620 625 630 | |
| ccc tcc acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc | 14691 |
| Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro | |
| 635 640 645 | |
| gga gcc ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac | 14739 |
| Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His | |
| 650 655 660 665 | |
| gtt ggc ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc | 14787 |
| Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala | |
| 670 675 680 | |
| ttc gcc tcc cgg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag | 14835 |
| Phe Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu | |
| 685 690 695 | |
| agc gat gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta | 14883 |
| Ser Asp Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val | |
| 700 705 710 | |
| acc cag ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc | 14931 |
| Thr Gln Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr | |
| 715 720 725 | |
| act cca tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc | 14979 |
| Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys | |
| 730 735 740 745 | |
| gag gtg ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca | 15027 |
| Glu Val Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro | |
| 750 755 760 | |
| cag ctg cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg | 15075 |
| Gln Leu Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly | |
| 765 770 775 | |
| gtc tgg cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct | 15123 |
| Val Trp Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala | |
| 780 785 790 | |
| gag atc act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct | 15171 |
| Glu Ile Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro | |
| 795 800 805 | |
| agg acc tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac | 15219 |
| Arg Thr Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr | |
| 810 815 820 825 | |

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|---|-------|
| acc acg ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg | 15267 |
| Thr Thr Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala | |
| 830 835 840 | |
| cta tgg agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg | 15315 |
| Leu Trp Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly | |
| 845 850 855 | |
| gac ttc cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg | 15363 |
| Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro | |
| 860 865 870 | |
| tgc cag gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc | 15411 |
| Cys Gln Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg | |
| 875 880 885 | |
| cta cat agg ttt gcg ccc ccc tgc aag ccc ttg ctg cgg gag gag gta | 15459 |
| Leu His Arg Phe Ala Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val | |
| 890 895 900 905 | |
| tca ttc aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct | 15507 |
| Ser Phe Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro | |
| 910 915 920 | |
| tgc gag ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat | 15555 |
| Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp | |
| 925 930 935 | |
| ccc tcc cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga | 15603 |
| Pro Ser His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly | |
| 940 945 950 | |
| tca ccc ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca | 15651 |
| Ser Pro Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro | |
| 955 960 965 | |
| tct ctc aag gca act tgc acc gct aac cat gac tcc cct gat gct gag | 15699 |
| Ser Leu Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu | |
| 970 975 980 985 | |
| ctc ata gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc | 15747 |
| Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile | |
| 990 995 1000 | |
| acc agg gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat | 15795 |
| Thr Arg Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp | |
| 1005 1010 1015 | |
| ccg ctt gtg gcg gag gag gac gag ccg gag atc tcc gta ccc gca gaa | 15843 |
| Pro Leu Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu | |
| 1020 1025 1030 | |
| atc ctg cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg | 15891 |
| Ile Leu Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala | |
| 1035 1040 1045 | |
| cgg ccg gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac | 15939 |
| Arg Pro Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp | |
| 1050 1055 1060 1065 | |

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|---|-------|
| tac gaa cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc | 15987 |
| Tyr Glu Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser | |
| 1070 1075 1080 | |
| cct cct gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa | 16035 |
| Pro Pro Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu | |
| 1085 1090 1095 | |
| tca acc cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc | 16083 |
| Ser Thr Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly | |
| 1100 1105 1110 | |
| agc tcc tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct | 16131 |
| Ser Ser Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser | |
| 1115 1120 1125 | |
| gag ccc gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat | 16179 |
| Glu Pro Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr | |
| 1130 1135 1140 1145 | |
| tcc tcc atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc | 16227 |
| Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser | |
| 1150 1155 1160 | |
| gac ggg tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc | 16275 |
| Asp Gly Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val | |
| 1165 1170 1175 | |
| gtg tgc tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg | 16323 |
| Val Cys Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro | |
| 1180 1185 1190 | |
| tgc gcc gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg | 16371 |
| Cys Ala Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser | |
| 1195 1200 1205 | |
| ttg cta cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct | 16419 |
| Leu Leu Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala | |
| 1210 1215 1220 1225 | |
| tgc caa agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac | 16467 |
| Cys Gln Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp | |
| 1230 1235 1240 | |
| agc cat tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa | 16515 |
| Ser His Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys | |
| 1245 1250 1255 | |
| gtg aag gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc | 16563 |
| Val Lys Ala Asn Leu Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro | |
| 1260 1265 1270 | |
| cca cac tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt | 16611 |
| Pro His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg | |
| 1275 1280 1285 | |
| tgc cat gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac | 16659 |
| Cys His Ala Arg Lys Ala Val Thr His Ile Asn Ser Val Trp Lys Asp | |
| 1290 1295 1300 1305 | |

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|---|-------|
| ctt ctg gaa gac aat gta aca cca ata gac act acc atc atg gct aag | 16707 |
| Leu Leu Glu Asp Asn Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys | |
| 1310 1315 1320 | |
| aac gag gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct | 16755 |
| Asn Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala | |
| 1325 1330 1335 | |
| cgt ctc atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg | 16803 |
| Arg Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met | |
| 1340 1345 1350 | |
| gct ttg tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc | 16851 |
| Ala Leu Tyr Asp Val Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser | |
| 1355 1360 1365 | |
| tcc tac gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg | 16899 |
| Ser Tyr Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val | |
| 1370 1375 1380 1385 | |
| caa gcg tgg aag tcc aag aaa acc cca atg ggg ttc tcg tat gat acc | 16947 |
| Gln Ala Trp Lys Ser Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr | |
| 1390 1395 1400 | |
| cgc tgc ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag | 16995 |
| Arg Cys Phe Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu | |
| 1405 1410 1415 | |
| gca atc tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc | 17043 |
| Ala Ile Tyr Gln Cys Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile | |
| 1420 1425 1430 | |
| aag tcc ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca | 17091 |
| Lys Ser Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser | |
| 1435 1440 1445 | |
| agg ggg gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg | 17139 |
| Arg Gly Glu Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu | |
| 1450 1455 1460 1465 | |
| aca act agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca | 17187 |
| Thr Thr Ser Cys Gly Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala | |
| 1470 1475 1480 | |
| gcc tgt cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc | 17235 |
| Ala Cys Arg Ala Ala Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly | |
| 1485 1490 1495 | |
| gac gac tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg | 17283 |
| Asp Asp Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala | |
| 1500 1505 1510 | |
| gcg agc ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc | 17331 |
| Ala Ser Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro | |
| 1515 1520 1525 | |
| cct ggg gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca | 17379 |
| Pro Gly Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser | |
| 1530 1535 1540 1545 | |

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|---|-------|
| tgc tcc tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc | 17427 |
| Cys Ser Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val | |
| 1550 1555 1560 | |
| tac tac ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg | 17475 |
| Tyr Tyr Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp | |
| 1565 1570 1575 | |
| gag aca gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc | 17523 |
| Glu Thr Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile | |
| 1580 1585 1590 | |
| atg ttt gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc | 17571 |
| Met Phe Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe | |
| 1595 1600 1605 | |
| ttt agc gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc | 17619 |
| Phe Ser Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys | |
| 1610 1615 1620 1625 | |
| gag atc tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca | 17667 |
| Glu Ile Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro | |
| 1630 1635 1640 | |
| atc att caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac | 17715 |
| Ile Ile Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr | |
| 1645 1650 1655 | |
| tct cca ggt gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg | 17763 |
| Ser Pro Gly Glu Ile Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly | |
| 1660 1665 1670 | |
| gta ccg ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct | 17811 |
| Val Pro Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala | |
| 1675 1680 1685 | |
| agg ctt ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc | 17859 |
| Arg Leu Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu | |
| 1690 1695 1700 1705 | |
| ttc aac tgg gca gta aga aca aag ctc aaa ctc act cca ata gcg gcc | 17907 |
| Phe Asn Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Ala Ala | |
| 1710 1715 1720 | |
| gct ggc cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg | 17955 |
| Ala Gly Gln Leu Asp Leu Ser Gly Trp Phe Thr Ala Gly Tyr Ser Gly | |
| 1725 1730 1735 | |
| gga gac att tat cac agc gtg tct cat gcc cgg ccc cgc tgg atc tgg | 18003 |
| Gly Asp Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp | |
| 1740 1745 1750 | |
| ttt tgc cta ctc ctg ctt gct gca ggg gta ggc atc tac ctc ctc ccc | 18051 |
| Phe Cys Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro | |
| 1755 1760 1765 | |
| aac cga tgaagggttg ggtaaacact ccggcctaaa aaaaaaaaaa aatctagaac | 18107 |
| Asn Arg | |
| 1770 | |

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tcgat

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: pd.deltaNS3NS5

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Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
 35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
 50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
 65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
 85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
 100 105 110

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
 115 120 125

Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
 130 135 140

Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
 145 150 155 160

Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala
 165 170 175

Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val
 180 185 190

Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe
 195 200 205

Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe
 210 215 220

Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile Thr Leu Pro Gln Asp
 225 230 235 240

Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr Gly Arg Gly Lys Pro
 245 250 255

Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg Pro Ser Gly Met Phe
 260 265 270
 Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr
 275 280 285
 Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu Arg Ala Tyr Met Asn
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 Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Gly
 305 310 315 320
 Val Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr
 325 330 335
 Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val Ala Tyr Gln Ala Thr
 340 345 350
 Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp
 355 360 365
 Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu
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 Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile Thr Leu Thr His Pro
 385 390 395 400
 Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala Asp Leu Glu Val Val
 405 410 415
 Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala
 420 425 430
 Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val Val Leu
 435 440 445
 Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Arg Glu
 450 455 460
 Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln
 465 470 475 480
 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
 485 490 495
 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
 500 505 510
 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
 515 520 525
 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn
 530 535 540
 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
 545 550 555 560
 Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val
 565 570 575

Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
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 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
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 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
 625 630 635 640
 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
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 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
 675 680 685
 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
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 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735
 Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
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 Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile
 770 775 780
 Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
 785 790 795 800
 Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
 805 810 815
 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
 820 825 830
 Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser Ala Glu
 835 840 845
 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
 850 855 860
 Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu
 865 870 875 880
 Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro
 885 890 895

Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
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 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
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 930 935 940
 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
 Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr
 965 970 975
 Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
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 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
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 Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro Asp Tyr Asn Pro Pro
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 Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Pro Arg
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 Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser Gly Ile
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 Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro Ala Pro Ser Gly Cys
 1125 1130 1135
 Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu
 1140 1145 1150
 Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val
 1155 1160 1165
 Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys Cys Ser Met Ser Tyr
 1170 1175 1180
 Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys
 1185 1190 1195 1200
 Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu
 1205 1210 1215

Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys Lys Val
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 Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu
 1235 1240 1245
 Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu Leu Ser
 1250 1255 1260
 Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys
 1265 1270 1275 1280
 Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys Ala Val
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 Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn Val Thr
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 Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys
 1380 1385 1390
 Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val
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 1410 1415 1420
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 Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr
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 1475 1480 1485
 Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys
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 Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala Phe Thr
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 Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro
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 Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp
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 Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg
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 Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr
 1620 1625 1630
 Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly
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 Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg
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 Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Ala Trp
 665 1670 1675 1680
 Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg Gly Gly
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 Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Arg Thr
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 Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly Gln Leu Asp Leu Ser
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 Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Val
 1730 1735 1740
 Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys Leu Leu Leu Leu Ala
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<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:

pd.deltaNS3NS5.pj

<220>

<221> CDS

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|------------|------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|------------------|-----|-------|-----|-------|
| gtattgattg | taattctgta | aatctatttc | ttaaacttct | taaattctac | ttttatagtt | 12600 | | | | | | | | | | |
| agtctttttt | ttagttttta | aacaccaaga | acttagtttc | gaataaacac | acataaacia | 12660 | | | | | | | | | | |
| acaagcttac | aaaacaaa | atg Met 1 | gct Ala 1 | gca Ala 5 | tat Tyr 5 | gca Ala 5 | gct Ala 5 | cag Gln 10 | ggc Gly 10 | tat Tyr 10 | aag Lys 10 | gtg Val 10 | | 12711 | | |
| cta | gta | ctc | aac | ccc | tct | gtt | gct | gca | aca | ctg | ggc | ttt | ggg | gct | tac | 12759 |
| Leu | Val | Leu | Asn | Pro | Ser | Val | Ala | Ala | Thr | Leu | Gly | Phe | Gly | Ala | Tyr | |
| | | | 15 | | | | | 20 | | | | | 25 | | | |
| atg | tcc | aag | gct | cat | ggg | atc | gat | cct | aac | atc | agg | acc | ggg | gtg | aga | 12807 |
| Met | Ser | Lys | Ala | His | Gly | Ile | Asp | Pro | Asn | Ile | Arg | Thr | Gly | Val | Arg | |
| | | 30 | | | | | 35 | | | | 40 | | | | | |
| aca | att | acc | act | ggc | agc | ccc | atc | acg | tac | tcc | acc | tac | ggc | aag | ttc | 12855 |
| Thr | Ile | Thr | Thr | Gly | Ser | Pro | Ile | Thr | Tyr | Ser | Thr | Tyr | Gly | Lys | Phe | |
| | 45 | | | | | 50 | | | | | 55 | | | | | |
| ctt | gcc | gac | ggc | ggg | tgc | tcg | ggg | ggc | gct | tat | gac | ata | ata | att | tgt | 12903 |
| Leu | Ala | Asp | Gly | Gly | Cys | Ser | Gly | Gly | Ala | Tyr | Asp | Ile | Ile | Ile | Cys | |
| | 60 | | | | 65 | | | | | 70 | | | | | 75 | |
| gac | gag | tgc | cac | tcc | acg | gat | gcc | aca | tcc | atc | ttg | ggc | att | ggc | act | 12951 |
| Asp | Glu | Cys | His | Ser | Thr | Asp | Ala | Thr | Ser | Ile | Leu | Gly | Ile | Gly | Thr | |
| | | | | 80 | | | | | 85 | | | | | 90 | | |
| gtc | ctt | gac | caa | gca | gag | act | gcg | ggg | gcg | aga | ctg | gtt | gtg | ctc | gcc | 12999 |
| Val | Leu | Asp | Gln | Ala | Glu | Thr | Ala | Gly | Ala | Arg | Leu | Val | Val | Leu | Ala | |
| | | | 95 | | | | | 100 | | | | | 105 | | | |
| acc | gcc | acc | cct | ccg | ggc | tcc | gtc | act | gtg | ccc | cat | ccc | aac | atc | gag | 13047 |
| Thr | Ala | Thr | Pro | Pro | Gly | Ser | Val | Thr | Val | Pro | His | Pro | Asn | Ile | Glu | |
| | | 110 | | | | | 115 | | | | | 120 | | | | |
| gag | gtt | gct | ctg | tcc | acc | acc | gga | gag | atc | cct | ttt | tac | ggc | aag | gct | 13095 |
| Glu | Val | Ala | Leu | Ser | Thr | Thr | Gly | Glu | Ile | Pro | Phe | Tyr | Gly | Lys | Ala | |
| | 125 | | | | | 130 | | | | | 135 | | | | | |
| atc | ccc | ctc | gaa | gta | atc | aag | ggg | ggg | aga | cat | ctc | atc | ttc | tgt | cat | 13143 |
| Ile | Pro | Leu | Glu | Val | Ile | Lys | Gly | Gly | Arg | His | Leu | Ile | Phe | Cys | His | |
| | 140 | | | | 145 | | | | | 150 | | | | | 155 | |
| tca | aag | aag | aag | tgc | gac | gaa | ctc | gcc | gca | aag | ctg | gtc | gca | ttg | ggc | 13191 |
| Ser | Lys | Lys | Lys | Cys | Asp | Glu | Leu | Ala | Ala | Lys | Leu | Val | Ala | Leu | Gly | |
| | | | | 160 | | | | | 165 | | | | | 170 | | |
| atc | aat | gcc | gtg | gcc | tac | tac | cgc | ggg | ctt | gac | gtg | tcc | gtc | atc | ccg | 13239 |
| Ile | Asn | Ala | Val | Ala | Tyr | Tyr | Arg | Gly | Leu | Asp | Val | Ser | Val | Ile | Pro | |
| | | 175 | | | | | | 180 | | | | | 185 | | | |
| acc | agc | ggc | gat | gtt | gtc | gtc | gtg | gca | acc | gat | gcc | ctc | atg | acc | ggc | 13287 |
| Thr | Ser | Gly | Asp | Val | Val | Val | Val | Ala | Thr | Asp | Ala | Leu | Met | Thr | Gly | |
| | | 190 | | | | | 195 | | | | | 200 | | | | |
| tat | acc | ggc | gac | ttc | gac | | | | | | | | | | | |

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|---|-------|
| cag aca gtc gat ttc agc ctt gac cct acc ttc acc att gag aca atc | 13383 |
| Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile | |
| 220 225 230 235 | |
| acg ctc ccc caa gat gct gtc tcc cgc act caa cgt cgg ggc agg act | 13431 |
| Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr | |
| 240 245 250 | |
| ggc agg ggg aag cca ggc atc tac aga ttt gtg gca ccg ggg gag cgc | 13479 |
| Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg | |
| 255 260 265 | |
| ccc tcc ggc atg ttc gac tcg tcc gtc ctc tgt gag tgc tat gac gca | 13527 |
| Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala | |
| 270 275 280 | |
| ggc tgt gct tgg tat gag ctc acg ccc gcc gag act aca gtt agg cta | 13575 |
| Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu | |
| 285 290 295 | |
| cga gcg tac atg aac acc ccg ggg ctt ccc gtg tgc cag gac cat ctt | 13623 |
| Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu | |
| 300 305 310 315 | |
| gaa ttt tgg gag ggc gtc ttt aca ggc ctc act cat ata gat gcc cac | 13671 |
| Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp Ala His | |
| 320 325 330 | |
| ttt cta tcc cag aca aag cag agt ggg gag aac ctt cct tac ctg gta | 13719 |
| Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val | |
| 335 340 345 | |
| gcg tac caa gcc acc gtg tgc gct agg gct caa gcc cct ccc cca tcg | 13767 |
| Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser | |
| 350 355 360 | |
| tgg gac cag atg tgg aag tgt ttg att cgc ctc aag ccc acc ctc cat | 13815 |
| Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His | |
| 365 370 375 | |
| ggg cca aca ccc ctg cta tac aga ctg ggc gct gtt cag aat gaa atc | 13863 |
| Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile | |
| 380 385 390 395 | |
| acc ctg acg cac cca gtc acc aaa tac atc atg aca tgc atg tcg gcc | 13911 |
| Thr Leu Thr His Pro Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala | |
| 400 405 410 | |
| gac ctg gag gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc gtc ctg | 13959 |
| Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu | |
| 415 420 425 | |
| gct gct ttg gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc ata gtg | 14007 |
| Ala Ala Leu Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val | |
| 430 435 440 | |
| ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa | 14055 |
| Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu | |
| 445 450 455 | |

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|---|-------|
| gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag cac tta | 14103 |
| Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu | |
| 460 465 470 475 | |
| ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag | 14151 |
| Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys | |
| 480 485 490 | |
| gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc | 14199 |
| Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala | |
| 495 500 505 | |
| cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag | 14247 |
| Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys | |
| 510 515 520 | |
| cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca | 14295 |
| His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser | |
| 525 530 535 | |
| acg ctg cct ggt aac ccc gcc att gct tca ttg atg gct ttt aca gct | 14343 |
| Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala | |
| 540 545 550 555 | |
| gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc aac ata | 14391 |
| Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile | |
| 560 565 570 | |
| ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act | 14439 |
| Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr | |
| 575 580 585 | |
| gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga | 14487 |
| Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly | |
| 590 595 600 | |
| ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg | 14535 |
| Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val | |
| 605 610 615 | |
| gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc | 14583 |
| Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser | |
| 620 625 630 635 | |
| acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc | 14631 |
| Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala | |
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| ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc | 14679 |
| Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly | |
| 655 660 665 | |
| ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc | 14727 |
| Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala | |
| 670 675 680 | |
| tcc cgg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat | 14775 |
| Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp | |
| 685 690 695 | |

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|---|-------|
| gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta acc cag | 14823 |
| Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln | |
| 700 705 710 715 | |
| ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc act cca | 14871 |
| Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro | |
| 720 725 730 | |
| tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg | 14919 |
| Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val | |
| 735 740 745 | |
| ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg | 14967 |
| Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu | |
| 750 755 760 | |
| cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg | 15015 |
| Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp | |
| 765 770 775 | |
| cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct gag atc | 15063 |
| Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile | |
| 780 785 790 795 | |
| act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc | 15111 |
| Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr | |
| 800 805 810 | |
| tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg | 15159 |
| Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr | |
| 815 820 825 | |
| ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg | 15207 |
| Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp | |
| 830 835 840 | |
| agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc | 15255 |
| Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe | |
| 845 850 855 | |
| cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag | 15303 |
| His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln | |
| 860 865 870 875 | |
| gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat | 15351 |
| Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His | |
| 880 885 890 | |
| agg ttt gcg ccc ccc tgc aag ccc ttg ctg ccg gag gag gta tca ttc | 15399 |
| Arg Phe Ala Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe | |
| 895 900 905 | |
| aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag | 15447 |
| Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu | |
| 910 915 920 | |
| ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc | 15495 |
| Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser | |
| 925 930 935 | |

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| cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc | 15543 |
| His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro | |
| 940 945 950 955 | |
| ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca tct ctc | 15591 |
| Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu | |
| 960 965 970 | |
| aag gca act tgc acc gct aac cat gac tcc cct gat gct gag ctc ata | 15639 |
| Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile | |
| 975 980 985 | |
| gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg | 15687 |
| Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg | |
| 990 995 1000 | |
| gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt | 15735 |
| Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu | |
| 1005 1010 1015 | |
| gtg gcg gag gag gac gag cgg gag atc tcc gta ccc gca gaa atc ctg | 15783 |
| Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu | |
| 1020 1025 1030 1035 | |
| cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg cgg ccg | 15831 |
| Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro | |
| 1040 1045 1050 | |
| gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa | 15879 |
| Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu | |
| 1055 1060 1065 | |
| cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct | 15927 |
| Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro | |
| 1070 1075 1080 | |
| gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa tca acc | 15975 |
| Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr | |
| 1085 1090 1095 | |
| cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc | 16023 |
| Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser | |
| 1100 1105 1110 1115 | |
| tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct gag ccc | 16071 |
| Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro | |
| 1120 1125 1130 | |
| gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc | 16119 |
| Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser | |
| 1135 1140 1145 | |
| atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg | 16167 |
| Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly | |
| 1150 1155 1160 | |
| tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc | 16215 |
| Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys | |
| 1165 1170 1175 | |

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| tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg tgc gcc | 16263 |
| Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala | |
| 1180 1185 1190 1195 | |
| gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta | 16311 |
| Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu | |
| 1200 1205 1210 | |
| cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct tgc caa | 16359 |
| Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln | |
| 1215 1220 1225 | |
| agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat | 16407 |
| Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His | |
| 1230 1235 1240 | |
| tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag | 16455 |
| Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys | |
| 1245 1250 1255 | |
| gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac | 16503 |
| Ala Asn Leu Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His | |
| 1260 1265 1270 1275 | |
| tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat | 16551 |
| Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His | |
| 1280 1285 1290 | |
| gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg | 16599 |
| Ala Arg Lys Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu | |
| 1295 1300 1305 | |
| gaa gac aat gta aca cca ata gac act acc atc atg gct aag aac gag | 16647 |
| Glu Asp Asn Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu | |
| 1310 1315 1320 | |
| gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc | 16695 |
| Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu | |
| 1325 1330 1335 | |
| atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg | 16743 |
| Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu | |
| 1340 1345 1350 1355 | |
| tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac | 16791 |
| Tyr Asp Val Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr | |
| 1360 1365 1370 | |
| gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg | 16839 |
| Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala | |
| 1375 1380 1385 | |
| tgg aag tcc aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc | 16887 |
| Trp Lys Ser Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys | |
| 1390 1395 1400 | |
| ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag gca atc | 16935 |
| Phe Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile | |
| 1405 1410 1415 | |

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| tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc | 16983 |
| Tyr Gln Cys Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser | |
| 1420 1425 1430 1435 | |
| ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg | 17031 |
| Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly | |
| 1440 1445 1450 | |
| gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act | 17079 |
| Glu Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr | |
| 1455 1460 1465 | |
| agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt | 17127 |
| Ser Cys Gly Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys | |
| 1470 1475 1480 | |
| cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac | 17175 |
| Arg Ala Ala Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp | |
| 1485 1490 1495 | |
| tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc | 17223 |
| Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser | |
| 1500 1505 1510 1515 | |
| ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg | 17271 |
| Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly | |
| 1520 1525 1530 | |
| gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc | 17319 |
| Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser | |
| 1535 1540 1545 | |
| tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac | 17367 |
| Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr | |
| 1550 1555 1560 | |
| ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca | 17415 |
| Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr | |
| 1565 1570 1575 | |
| gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc atg ttt | 17463 |
| Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe | |
| 1580 1585 1590 1595 | |
| gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc ttt agc | 17511 |
| Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser | |
| 1600 1605 1610 | |
| gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc gag atc | 17559 |
| Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile | |
| 1615 1620 1625 | |
| tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca atc att | 17607 |
| Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile | |
| 1630 1635 1640 | |
| caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac tct cca | 17655 |
| Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro | |
| 1645 1650 1655 | |

ggt gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg gta ccg 17703
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ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct agg ctt 17751
 Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu
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ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc ttc aac 17799
 Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn
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cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg gga gac 17895
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 Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys
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 Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
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<211> 1771

<212> PRT

<213> Artificial Sequence

<220>

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Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
 100 105 110
 Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
 115 120 125
 Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
 130 135 140
 Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
 145 150 155 160
 Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala
 165 170 175
 Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val
 180 185 190
 Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe
 195 200 205
 Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe
 210 215 220
 Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile Thr Leu Pro Gln Asp
 225 230 235 240
 Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr Gly Arg Gly Lys Pro
 245 250 255
 Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg Pro Ser Gly Met Phe
 260 265 270
 Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr
 275 280 285
 Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu Arg Ala Tyr Met Asn
 290 295 300
 Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Gly
 305 310 315 320
 Val Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr
 325 330 335
 Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val Ala Tyr Gln Ala Thr
 340 345 350
 Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp
 355 360 365
 Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu
 370 375 380
 Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile Thr Leu Thr His Pro
 385 390 395 400
 Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala Asp Leu Glu Val Val
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Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala
 420 425 430
 Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val Val Leu
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 Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Arg Glu
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 Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln
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 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
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 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
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 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
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 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
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 595 600 605
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 625 630 635 640
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 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
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 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu
 705 710 715 720
 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735

Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
 755 760 765
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 770 775 780
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 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
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 835 840 845
 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
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 Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu
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 Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
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 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
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 930 935 940
 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
 Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr
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 995 1000 1005
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Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val Val His
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 Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser Gly Ile
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 Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys
 1185 1190 1195 1200
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 Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu
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acaagcttac aaaacaaa atg gct gca tat gca gct cag ggc tat aag gtg 12711
Met Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val
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Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr
15 20 25
atg tcc aag gct cat ggg atc gat cct aac atc agg acc ggg gtg aga 12807
Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg
30 35 40
aca att acc act ggc agc ccc atc acg tac tcc acc tac ggc aag ttc 12855
Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe
45 50 55
ctt gcc gac ggc ggg tgc tcg ggg ggc gct tat gac ata ata att tgt 12903
Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys
60 65 70 75
gac gag tgc cac tcc acg gat gcc aca tcc atc ttg ggc att ggc act 12951
Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr
80 85 90
gtc ctt gac caa gca gag act gcg ggg gcg aga ctg gtt gtg ctc gcc 12999

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|
| Val | Leu | Asp | Gln | Ala | Glu | Thr | Ala | Gly | Ala | Arg | Leu | Val | Val | Leu | Ala | |
| | | | 95 | | | | | 100 | | | | | 105 | | | |
| acc | gcc | acc | cct | ccg | ggc | tcc | gtc | act | gtg | ccc | cat | ccc | aac | atc | gag | 13047 |
| Thr | Ala | Thr | Pro | Pro | Gly | Ser | Val | Thr | Val | Pro | His | Pro | Asn | Ile | Glu | |
| | | 110 | | | | | 115 | | | | | 120 | | | | |
| gag | gtt | gct | ctg | tcc | acc | acc | gga | gag | atc | cct | ttt | tac | ggc | aag | gct | 13095 |
| Glu | Val | Ala | Leu | Ser | Thr | Thr | Gly | Glu | Ile | Pro | Phe | Tyr | Gly | Lys | Ala | |
| | | 125 | | | | | 130 | | | | 135 | | | | | |
| atc | ccc | ctc | gaa | gta | atc | aag | ggg | ggg | aga | cat | ctc | atc | ttc | tgt | cat | 13143 |
| Ile | Pro | Leu | Glu | Val | Ile | Lys | Gly | Gly | Arg | His | Leu | Ile | Phe | Cys | His | |
| | 140 | | | | | 145 | | | | 150 | | | | | 155 | |
| tca | aag | aag | aag | tgc | gac | gaa | ctc | gcc | gca | aag | ctg | gtc | gca | ttg | ggc | 13191 |
| Ser | Lys | Lys | Lys | Cys | Asp | Glu | Leu | Ala | Ala | Lys | Leu | Val | Ala | Leu | Gly | |
| | | | | 160 | | | | | 165 | | | | | 170 | | |
| atc | aat | gcc | gtg | gcc | tac | tac | cgc | ggt | ctt | gac | gtg | tcc | gtc | atc | ccg | 13239 |
| Ile | Asn | Ala | Val | Ala | Tyr | Tyr | Arg | Gly | Leu | Asp | Val | Ser | Val | Ile | Pro | |
| | | 175 | | | | | | 180 | | | | | 185 | | | |
| acc | agc | ggc | gat | gtt | gtc | gtc | gtg | gca | acc | gat | gcc | ctc | atg | acc | ggc | 13287 |
| Thr | Ser | Gly | Asp | Val | Val | Val | Val | Ala | Thr | Asp | Ala | Leu | Met | Thr | Gly | |
| | | 190 | | | | | 195 | | | | | 200 | | | | |
| tat | acc | ggc | gac | ttc | gac | tcg | gtg | ata | gac | tgc | aat | acg | tgt | gtc | acc | 13335 |
| Tyr | Thr | Gly | Asp | Phe | Asp | Ser | Val | Ile | Asp | Cys | Asn | Thr | Cys | Val | Thr | |
| | 205 | | | | | 210 | | | | | 215 | | | | | |
| cag | aca | gtc | gat | ttc | agc | ctt | gac | cct | acc | ttc | acc | att | gag | aca | atc | 13383 |
| Gln | Thr | Val | Asp | Phe | Ser | Leu | Asp | Pro | Thr | Phe | Thr | Ile | Glu | Thr | Ile | |
| | 220 | | | | 225 | | | | | 230 | | | | | 235 | |
| acg | ctc | ccc | caa | gat | gct | gtc | tcc | cgc | act | caa | cgt | cgg | ggc | agg | act | 13431 |
| Thr | Leu | Pro | Gln | Asp | Ala | Val | Ser | Arg | Thr | Gln | Arg | Arg | Gly | Arg | Thr | |
| | | | 240 | | | | | 245 | | | | | 250 | | | |
| ggc | agg | ggg | aag | cca | ggc | atc | tac | aga | ttt | gtg | gca | ccg | ggg | gag | cgc | 13479 |
| Gly | Arg | Gly | Lys | Pro | Gly | Ile | Tyr | Arg | Phe | Val | Ala | Pro | Gly | Glu | Arg | |
| | | 255 | | | | | | 260 | | | | 265 | | | | |
| ccc | tcc | ggc | atg | ttc | gac | tcg | tcc | gtc | ctc | tgt | gag | tgc | tat | gac | gca | 13527 |
| Pro | Ser | Gly | Met | Phe | Asp | Ser | Ser | Val | Leu | Cys | Glu | Cys | Tyr | Asp | Ala | |
| | | 270 | | | | | 275 | | | | | 280 | | | | |
| ggc | tgt | gct | tgg | tat | gag | ctc | acg | ccc | gcc | gag | act | aca | gtt | agg | cta | 13575 |
| Gly | Cys | Ala | Trp | Tyr | Glu | Leu | Thr | Pro | Ala | Glu | Thr | Thr | Val | Arg | Leu | |
| | 285 | | | | | 290 | | | | | 295 | | | | | |
| cga | gcg | tac | atg | aac | acc | ccg | ggg | ctt | ccc | gtg | tgc | cag | gac | cat | ctt | 13623 |
| Arg | Ala | Tyr | Met | Asn | Thr | Pro | Gly | Leu | Pro | Val | Cys | Gln | Asp | His | Leu | |
| | 300 | | | | 305 | | | | | 310 | | | | | 315 | |
| gaa | ttt | tgg | gag | ggc | gtc | ttt | aca | ggc | ctc | act | cat | ata | gat | gcc | cac | 13671 |
| Glu | Phe | Trp | Glu | Gly | Val | Phe | Thr | Gly | Leu | Thr | His | Ile | Asp | Ala | His | |
| | | | 320 | | | | | | 325 | | | | | 330 | | |

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|---|-------|
| ttt cta tcc cag aca aag cag agt ggg gag aac ctt cct tac ctg gta | 13719 |
| Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val | |
| 335 340 345 | |
| gcg tac caa gcc acc gtg tgc gct agg gct caa gcc cct ccc cca tgc | 13767 |
| Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser | |
| 350 355 360 | |
| tgg gac cag atg tgg aag tgt ttg att cgc ctc aag ccc acc ctc cat | 13815 |
| Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His | |
| 365 370 375 | |
| ggg cca aca ccc ctg cta tac aga ctg ggc gct gtt cag aat gaa atc | 13863 |
| Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile | |
| 380 385 390 395 | |
| acc ctg acg cac cca gtc acc aaa tac atc atg aca tgc atg tgc gcc | 13911 |
| Thr Leu Thr His Pro Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala | |
| 400 405 410 | |
| gac ctg gag gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc gtc ctg | 13959 |
| Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu | |
| 415 420 425 | |
| gct gct ttg gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc ata gtg | 14007 |
| Ala Ala Leu Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val | |
| 430 435 440 | |
| ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa | 14055 |
| Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu | |
| 445 450 455 | |
| gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag cac tta | 14103 |
| Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu | |
| 460 465 470 475 | |
| ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag | 14151 |
| Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys | |
| 480 485 490 | |
| gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc | 14199 |
| Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala | |
| 495 500 505 | |
| cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag | 14247 |
| Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys | |
| 510 515 520 | |
| cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca | 14295 |
| His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser | |
| 525 530 535 | |
| acg ctg cct ggt aac ccc gcc att gct tca ttg atg gct ttt aca gct | 14343 |
| Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala | |
| 540 545 550 555 | |
| gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc aac ata | 14391 |
| Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile | |
| 560 565 570 | |

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|---|-------|
| ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act | 14439 |
| Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr | |
| 575 580 585 | |
| gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga | 14487 |
| Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly | |
| 590 595 600 | |
| ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg | 14535 |
| Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val | |
| 605 610 615 | |
| gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc | 14583 |
| Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser | |
| 620 625 630 635 | |
| acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc | 14631 |
| Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala | |
| 640 645 650 | |
| ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc | 14679 |
| Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly | |
| 655 660 665 | |
| ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc | 14727 |
| Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala | |
| 670 675 680 | |
| tcc cgg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat | 14775 |
| Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp | |
| 685 690 695 | |
| gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta acc cag | 14823 |
| Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln | |
| 700 705 710 715 | |
| ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc act cca | 14871 |
| Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro | |
| 720 725 730 | |
| tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg | 14919 |
| Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val | |
| 735 740 745 | |
| ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg | 14967 |
| Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu | |
| 750 755 760 | |
| cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg | 15015 |
| Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp | |
| 765 770 775 | |
| cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct gag atc | 15063 |
| Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile | |
| 780 785 790 795 | |
| act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc | 15111 |
| Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr | |
| 800 805 810 | |

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|---|-------|
| tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg | 15159 |
| Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr | |
| 815 820 825 | |
| ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg | 15207 |
| Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp | |
| 830 835 840 | |
| agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc | 15255 |
| Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe | |
| 845 850 855 | |
| cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag | 15303 |
| His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln | |
| 860 865 870 875 | |
| gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat | 15351 |
| Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His | |
| 880 885 890 | |
| agg ttt gcg ccc ccc tgc aag ccc ttg ctg cgg gag gag gta tca ttc | 15399 |
| Arg Phe Ala Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe | |
| 895 900 905 | |
| aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag | 15447 |
| Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu | |
| 910 915 920 | |
| ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc | 15495 |
| Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser | |
| 925 930 935 | |
| cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc | 15543 |
| His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro | |
| 940 945 950 955 | |
| ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca tct ctc | 15591 |
| Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu | |
| 960 965 970 | |
| aag gca act tgc acc gct aac cat gac tcc cct gat gct gag ctc ata | 15639 |
| Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile | |
| 975 980 985 | |
| gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg | 15687 |
| Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg | |
| 990 995 1000 | |
| gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt | 15735 |
| Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu | |
| 1005 1010 1015 | |
| gtg gcg gag gag gac gag cgg gag atc tcc gta ccc gca gaa atc ctg | 15783 |
| Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu | |
| 1020 1025 1030 1035 | |
| cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg cgg ccg | 15831 |
| Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro | |
| 1040 1045 1050 | |

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|---|-------|
| gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu 1055 1060 1065 | 15879 |
| cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro 1070 1075 1080 | 15927 |
| gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa tca acc Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr 1085 1090 1095 | 15975 |
| cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser 1100 1105 1110 1115 | 16023 |
| tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct gag ccc Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro 1120 1125 1130 | 16071 |
| gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser 1135 1140 1145 | 16119 |
| atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly 1150 1155 1160 | 16167 |
| tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys 1165 1170 1175 | 16215 |
| tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg tgc gcc Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala 1180 1185 1190 1195 | 16263 |
| gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu 1200 1205 1210 | 16311 |
| cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct tgc caa Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln 1215 1220 1225 | 16359 |
| agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His 1230 1235 1240 | 16407 |
| tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys 1245 1250 1255 | 16455 |
| gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac Ala Asn Leu Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His 1260 1265 1270 1275 | 16503 |
| tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His 1280 1285 1290 | 16551 |

gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg 16599
 Ala Arg Lys Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu
 1295 1300 1305

gaa gac aat gta aca cca ata gac act acc atc atg gct aag aac gag 16647
 Glu Asp Asn Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu
 1310 1315 1320

gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc 16695
 Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu
 1325 1330 1335

atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg 16743
 Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu
 1340 1345 1350 1355

tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac 16791
 Tyr Asp Val Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr
 1360 1365 1370

gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg 16839
 Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala
 1375 1380 1385

tgg aag tcc aag aaa acc cca atg ggg ttc tgc tat gat acc cgc tgc 16887
 Trp Lys Ser Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys
 1390 1395 1400

ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag gca atc 16935
 Phe Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile
 1405 1410 1415

tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc 16983
 Tyr Gln Cys Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser
 1420 1425 1430 1435

ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg 17031
 Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly
 1440 1445 1450

gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act 17079
 Glu Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr
 1455 1460 1465

agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt 17127
 Ser Cys Gly Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys
 1470 1475 1480

cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac 17175
 Arg Ala Ala Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp
 1485 1490 1495

tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc 17223
 Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser
 1500 1505 1510 1515

ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg 17271
 Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly
 1520 1525 1530

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|---|-------|
| gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc | 17319 |
| Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser | |
| 1535 1540 1545 | |
| tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac | 17367 |
| Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr | |
| 1550 1555 1560 | |
| ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca | 17415 |
| Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr | |
| 1565 1570 1575 | |
| gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc atg ttt | 17463 |
| Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe | |
| 1580 1585 1590 1595 | |
| gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc ttt agc | 17511 |
| Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser | |
| 1600 1605 1610 | |
| gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc gag atc | 17559 |
| Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile | |
| 1615 1620 1625 | |
| tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca atc att | 17607 |
| Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile | |
| 1630 1635 1640 | |
| caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac tct cca | 17655 |
| Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro | |
| 1645 1650 1655 | |
| ggg gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg gta ccg | 17703 |
| Gly Glu Ile Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro | |
| 1660 1665 1670 1675 | |
| ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct agg ctt | 17751 |
| Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu | |
| 1680 1685 1690 | |
| ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc ttc aac | 17799 |
| Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn | |
| 1695 1700 1705 | |
| tgg gca gta aga aca aag ctc aaa ctc act cca ata gcg gcc gct ggc | 17847 |
| Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly | |
| 1710 1715 1720 | |
| cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg gga gac | 17895 |
| Gln Leu Asp Leu Ser Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp | |
| 1725 1730 1735 | |
| att tat cac agc gtg tct cat gcc cgg ccc cgc tgg atc tgg ttt tgc | 17943 |
| Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys | |
| 1740 1745 1750 1755 | |
| cta ctc ctg ctt gct gca ggg gta ggc atc tac ctc ctc ccc aac cga | 17991 |
| Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg | |
| 1760 1765 1770 | |

atg agc acg aat cct aaa cct caa aga aag acc aaa cgt aac acc aac 18039
 Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn
 1775 1780 1785

cgg cgg ccg cag gac gtc aag ttc ccg ggt ggc ggt cag atc gtt ggt 18087
 Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
 1790 1795 1800

gga gtt tac ttg ttg ccg cgc agg ggc cct aga ttg ggt gtg cgc gcg 18135
 Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala
 1805 1810 1815

acg aga aag act tcc gag cgg tcg caa cct cga ggt aga cgt cag cct 18183
 Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
 1820 1825 1830 1835

atc ccc aag gct cgt cgg ccc gag ggc agg acc tgg gct cag ccc ggg 18231
 Ile Pro Lys Ala Arg Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly
 1840 1845 1850

tac cct tgg ccc ctc tat ggc aat gag ggc tgc ggg tgg gcg gga tgg 18279
 Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp
 1855 1860 1865

ctc ctg tct ccc cgt ggc tct cgg cct agc tgg ggc ccc aca gac ccc 18327
 Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro
 1870 1875 1880

cgg cgt agg tcg cgc aat ttg ggt aag taatagtcga ctttgttccc 18374
 Arg Arg Arg Ser Arg Asn Leu Gly Lys
 1885 1890

actgtacttt tagctcgtac aaaatacaat atacttttca tttctccgta aacaacatgt 18434
 tttcccatgt aatatccttt tctatttttc gttccggtac caactttaca catactttat 18494
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<211> 1892

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:
pd.delta.NS3NS5.pj.core121

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Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His
20 25 30

Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala

| 85 | | | | | | | | | | 90 | | | | | 95 | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|
| Glu | Thr | Ala | Gly | Ala | Arg | Leu | Val | Val | Leu | Ala | Thr | Ala | Thr | Pro | Pro | | | | |
| | | | 100 | | | | | | 105 | | | | | 110 | | | | | |
| Gly | Ser | Val | Thr | Val | Pro | His | Pro | Asn | Ile | Glu | Glu | Val | Ala | Leu | Ser | | | | |
| | | | 115 | | | | 120 | | | | | | 125 | | | | | | |
| Thr | Thr | Gly | Glu | Ile | Pro | Phe | Tyr | Gly | Lys | Ala | Ile | Pro | Leu | Glu | Val | | | | |
| | | | 130 | | | | 135 | | | | | | 140 | | | | | | |
| Ile | Lys | Gly | Gly | Arg | His | Leu | Ile | Phe | Cys | His | Ser | Lys | Lys | Lys | Cys | | | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | | | |
| Asp | Glu | Leu | Ala | Ala | Lys | Leu | Val | Ala | Leu | Gly | Ile | Asn | Ala | Val | Ala | | | | |
| | | | | 165 | | | | | 170 | | | | | 175 | | | | | |
| Tyr | Tyr | Arg | Gly | Leu | Asp | Val | Ser | Val | Ile | Pro | Thr | Ser | Gly | Asp | Val | | | | |
| | | | 180 | | | | | 185 | | | | | | 190 | | | | | |
| Val | Val | Val | Ala | Thr | Asp | Ala | Leu | Met | Thr | Gly | Tyr | Thr | Gly | Asp | Phe | | | | |
| | | | 195 | | | | 200 | | | | | | 205 | | | | | | |
| Asp | Ser | Val | Ile | Asp | Cys | Asn | Thr | Cys | Val | Thr | Gln | Thr | Val | Asp | Phe | | | | |
| | | 210 | | | | 215 | | | | | 220 | | | | | | | | |
| Ser | Leu | Asp | Pro | Thr | Phe | Thr | Ile | Glu | Thr | Ile | Thr | Leu | Pro | Gln | Asp | | | | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | | | | |
| Ala | Val | Ser | Arg | Thr | Gln | Arg | Arg | Gly | Arg | Thr | Gly | Arg | Gly | Lys | Pro | | | | |
| | | | | 245 | | | | | 250 | | | | | 255 | | | | | |
| Gly | Ile | Tyr | Arg | Phe | Val | Ala | Pro | Gly | Glu | Arg | Pro | Ser | Gly | Met | Phe | | | | |
| | | | 260 | | | | | 265 | | | | | | 270 | | | | | |
| Asp | Ser | Ser | Val | Leu | Cys | Glu | Cys | Tyr | Asp | Ala | Gly | Cys | Ala | Trp | Tyr | | | | |
| | | | 275 | | | | 280 | | | | | | 285 | | | | | | |
| Glu | Leu | Thr | Pro | Ala | Glu | Thr | Thr | Val | Arg | Leu | Arg | Ala | Tyr | Met | Asn | | | | |
| | | | 290 | | | 295 | | | | | | 300 | | | | | | | |
| Thr | Pro | Gly | Leu | Pro | Val | Cys | Gln | Asp | His | Leu | Glu | Phe | Trp | Glu | Gly | | | | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | | | | |
| Val | Phe | Thr | Gly | Leu | Thr | His | Ile | Asp | Ala | His | Phe | Leu | Ser | Gln | Thr | | | | |
| | | | | 325 | | | | | 330 | | | | | 335 | | | | | |
| Lys | Gln | Ser | Gly | Glu | Asn | Leu | Pro | Tyr | Leu | Val | Ala | Tyr | Gln | Ala | Thr | | | | |
| | | | 340 | | | | | 345 | | | | | 350 | | | | | | |
| Val | Cys | Ala | Arg | Ala | Gln | Ala | Pro | Pro | Pro | Ser | Trp | Asp | Gln | Met | Trp | | | | |
| | | | 355 | | | | 360 | | | | | | 365 | | | | | | |
| Lys | Cys | Leu | Ile | Arg | Leu | Lys | Pro | Thr | Leu | His | Gly | Pro | Thr | Pro | Leu | | | | |
| | | | 370 | | | 375 | | | | | | 380 | | | | | | | |
| Leu | Tyr | Arg | Leu | Gly | Ala | Val | Gln | Asn | Glu | Ile | Thr | Leu | Thr | His | Pro | | | | |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 | | | | |

Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala Asp Leu Glu Val Val
 405 410 415
 Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala
 420 425 430
 Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val Val Leu
 435 440 445
 Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Arg Glu
 450 455 460
 Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln
 465 470 475 480
 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
 485 490 495
 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
 500 505 510
 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
 515 520 525
 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn
 530 535 540
 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
 545 550 555 560
 Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val
 565 570 575
 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
 580 585 590
 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
 610 615 620
 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
 625 630 635 640
 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
 675 680 685
 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu
 705 710 715 720

His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735
 Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
 755 760 765
 Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile
 770 775 780
 Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
 785 790 795 800
 Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
 805 810 815
 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
 820 825 830
 Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser Ala Glu
 835 840 845
 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
 850 855 860
 Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu
 865 870 875 880
 Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro
 885 890 895
 Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
 900 905 910
 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
 Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu
 930 935 940
 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
 Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr
 965 970 975
 Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
 980 985 990
 Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn
 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
 1010 1015 1020
 Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Arg Arg
 1025 1030 1035 1040

Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro Asp Tyr Asn Pro Pro
 1045 1050 1055
 Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val Val His
 1060 1065 1070
 Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Arg
 1075 1080 1085
 Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr Leu Ser Thr Ala Leu
 1090 1095 1100
 Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser Gly Ile
 1105 1110 1115 1120
 Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro Ala Pro Ser Gly Cys
 1125 1130 1135
 Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu
 1140 1145 1150
 Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val
 1155 1160 1165
 Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys Cys Ser Met Ser Tyr
 1170 1175 1180
 Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys
 1185 1190 1195 1200
 Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu
 1205 1210 1215
 Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys Lys Val
 1220 1225 1230
 Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu
 1235 1240 1245
 Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu Leu Ser
 1250 1255 1260
 Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys
 1265 1270 1275 1280
 Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys Ala Val
 1285 1290 1295
 Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn Val Thr
 1300 1305 1310
 Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln
 1315 1320 1325
 Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp
 1330 1335 1340
 Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Thr
 1345 1350 1355 1360

Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser
 1365 1370 1375
 Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys
 1380 1385 1390
 Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val
 1395 1400 1405
 Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys Cys Asp
 1410 1415 1420
 Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu Arg Leu
 425 1430 1435 1440
 Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr
 1445 1450 1455
 Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr
 1460 1465 1470
 Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala Gly Leu
 1475 1480 1485
 Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys
 1490 1495 1500
 Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser Leu Arg Ala Phe Thr
 505 1510 1515 1520
 Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro
 1525 1530 1535
 Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val
 1540 1545 1550
 Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro
 1555 1560 1565
 Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro
 1570 1575 1580
 Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp
 585 1590 1595 1600
 Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg
 1605 1610 1615
 Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr
 1620 1625 1630
 Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly
 1635 1640 1645
 Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg
 1650 1655 1660
 Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Ala Trp
 665 1670 1675 1680

Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg Gly Gly
 1685 1690 1695

Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Arg Thr
 1700 1705 1710

Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly Gln Leu Asp Leu Ser
 1715 1720 1725

Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Val
 1730 1735 1740

Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys Leu Leu Leu Leu Ala
 745 1750 1755 1760

Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg Met Ser Thr Asn Pro
 1765 1770 1775

Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn Arg Arg Pro Gln Asp
 1780 1785 1790

Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly Gly Val Tyr Leu Leu
 1795 1800 1805

Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala Thr Arg Lys Thr Ser
 1810 1815 1820

Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro Ile Pro Lys Ala Arg
 825 1830 1835 1840

Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly Tyr Pro Trp Pro Leu
 1845 1850 1855

Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp Leu Leu Ser Pro Arg
 1860 1865 1870

Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro Arg Arg Arg Ser Arg
 1875 1880 1885

Asn Leu Gly Lys
 1890

<210> 14

<211> 20316

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:
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<220>

<221> CDS

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cggatcaacg ttcttaatat cgctgaatct tccacaattg atgaaagtag ctaggaagag 180
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| ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa | 14055 |
| Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu | |
| 445 450 455 | |
| gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag cac tta | 14103 |
| Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu | |
| 460 465 470 475 | |

| | |
|---|-------|
| ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag | 14151 |
| Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys | |
| 480 485 490 | |
| gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc | 14199 |
| Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala | |
| 495 500 505 | |
| cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag | 14247 |
| Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys | |
| 510 515 520 | |
| cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca | 14295 |
| His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser | |
| 525 530 535 | |
| acg ctg cct ggt aac ccc gcc att gct tca ttg atg gct ttt aca gct | 14343 |
| Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala | |
| 540 545 550 555 | |
| gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc aac ata | 14391 |
| Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile | |
| 560 565 570 | |
| ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act | 14439 |
| Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr | |
| 575 580 585 | |
| gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga | 14487 |
| Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly | |
| 590 595 600 | |
| ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg | 14535 |
| Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val | |
| 605 610 615 | |
| gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc | 14583 |
| Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser | |
| 620 625 630 635 | |
| acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc | 14631 |
| Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala | |
| 640 645 650 | |
| ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc | 14679 |
| Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly | |
| 655 660 665 | |
| ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc | 14727 |
| Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala | |
| 670 675 680 | |
| tcc cgg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat | 14775 |
| Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp | |
| 685 690 695 | |
| gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta acc cag | 14823 |
| Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln | |
| 700 705 710 715 | |

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| ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc act cca | 14871 |
| Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro | |
| 720 725 730 | |
| tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg | 14919 |
| Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val | |
| 735 740 745 | |
| ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg | 14967 |
| Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu | |
| 750 755 760 | |
| cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg | 15015 |
| Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp | |
| 765 770 775 | |
| cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct gag atc | 15063 |
| Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile | |
| 780 785 790 795 | |
| act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc | 15111 |
| Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr | |
| 800 805 810 | |
| tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg | 15159 |
| Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr | |
| 815 820 825 | |
| ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg | 15207 |
| Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp | |
| 830 835 840 | |
| agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc | 15255 |
| Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe | |
| 845 850 855 | |
| cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag | 15303 |
| His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln | |
| 860 865 870 875 | |
| gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat | 15351 |
| Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His | |
| 880 885 890 | |
| agg ttt gcg ccc ccc tgc aag ccc ttg ctg ccg gag gag gta tca ttc | 15399 |
| Arg Phe Ala Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe | |
| 895 900 905 | |
| aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag | 15447 |
| Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu | |
| 910 915 920 | |
| ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc | 15495 |
| Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser | |
| 925 930 935 | |
| cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc | 15543 |
| His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro | |
| 940 945 950 955 | |

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| ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca tct ctc | 15591 |
| Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu | |
| 960 965 970 | |
| aag gca act tgc acc gct aac cat gac tcc cct gat gct gag ctc ata | 15639 |
| Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile | |
| 975 980 985 | |
| gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg | 15687 |
| Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg | |
| 990 995 1000 | |
| gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt | 15735 |
| Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu | |
| 1005 1010 1015 | |
| gtg gcg gag gag gac gag cgg gag atc tcc gta ccc gca gaa atc ctg | 15783 |
| Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu | |
| 1020 1025 1030 1035 | |
| cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg cgg ccg | 15831 |
| Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro | |
| 1040 1045 1050 | |
| gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa | 15879 |
| Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu | |
| 1055 1060 1065 | |
| cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct | 15927 |
| Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro | |
| 1070 1075 1080 | |
| gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa tca acc | 15975 |
| Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr | |
| 1085 1090 1095 | |
| cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc | 16023 |
| Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser | |
| 1100 1105 1110 1115 | |
| tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct gag ccc | 16071 |
| Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro | |
| 1120 1125 1130 | |
| gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc | 16119 |
| Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser | |
| 1135 1140 1145 | |
| atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg | 16167 |
| Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly | |
| 1150 1155 1160 | |
| tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc | 16215 |
| Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys | |
| 1165 1170 1175 | |
| tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg tgc gcc | 16263 |
| Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala | |
| 1180 1185 1190 1195 | |

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| gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta | 16311 |
| Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu | |
| 1200 1205 1210 | |
| cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct tgc caa | 16359 |
| Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln | |
| 1215 1220 1225 | |
| agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat | 16407 |
| Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His | |
| 1230 1235 1240 | |
| tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag | 16455 |
| Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys | |
| 1245 1250 1255 | |
| gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac | 16503 |
| Ala Asn Leu Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His | |
| 1260 1265 1270 1275 | |
| tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat | 16551 |
| Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His | |
| 1280 1285 1290 | |
| gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg | 16599 |
| Ala Arg Lys Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu | |
| 1295 1300 1305 | |
| gaa gac aat gta aca cca ata gac act acc atc atg gct aag aac gag | 16647 |
| Glu Asp Asn Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu | |
| 1310 1315 1320 | |
| gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc | 16695 |
| Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu | |
| 1325 1330 1335 | |
| atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg | 16743 |
| Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu | |
| 1340 1345 1350 1355 | |
| tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac | 16791 |
| Tyr Asp Val Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr | |
| 1360 1365 1370 | |
| gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg | 16839 |
| Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala | |
| 1375 1380 1385 | |
| tgg aag tcc aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc | 16887 |
| Trp Lys Ser Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys | |
| 1390 1395 1400 | |
| ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag gca atc | 16935 |
| Phe Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile | |
| 1405 1410 1415 | |
| tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc | 16983 |
| Tyr Gln Cys Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser | |
| 1420 1425 1430 1435 | |

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|---|-------|
| ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly 1440 1445 1450 | 17031 |
| gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act Glu Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr 1455 1460 1465 | 17079 |
| agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt Ser Cys Gly Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys 1470 1475 1480 | 17127 |
| cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac Arg Ala Ala Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp 1485 1490 1495 | 17175 |
| tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser 1500 1505 1510 1515 | 17223 |
| ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly 1520 1525 1530 | 17271 |
| gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser 1535 1540 1545 | 17319 |
| tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr 1550 1555 1560 | 17367 |
| ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr 1565 1570 1575 | 17415 |
| gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc atg ttt Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe 1580 1585 1590 1595 | 17463 |
| gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc ttt agc Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser 1600 1605 1610 | 17511 |
| gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc gag atc Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile 1615 1620 1625 | 17559 |
| tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca atc att Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile 1630 1635 1640 | 17607 |
| caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac tct cca Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro 1645 1650 1655 | 17655 |
| ggg gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg gta ccg Gly Glu Ile Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro 1660 1665 1670 1675 | 17703 |

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| ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct agg ctt | 17751 |
| Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu | |
| 1680 1685 1690 | |
| ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc ttc aac | 17799 |
| Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn | |
| 1695 1700 1705 | |
| tgg gca gta aga aca aag ctc aaa ctc act cca ata gcg gcc gct ggc | 17847 |
| Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly | |
| 1710 1715 1720 | |
| cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg gga gac | 17895 |
| Gln Leu Asp Leu Ser Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp | |
| 1725 1730 1735 | |
| att tat cac agc gtg tct cat gcc cgg ccc cgc tgg atc tgg ttt tgc | 17943 |
| Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys | |
| 1740 1745 1750 1755 | |
| cta ctc ctg ctt gct gca ggg gta ggc atc tac ctc ctc ccc aac cga | 17991 |
| Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg | |
| 1760 1765 1770 | |
| atg agc acg aat cct aaa cct caa aga aag acc aaa cgt aac acc aac | 18039 |
| Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn | |
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| cgg cgg ccg cag gac gtc aag ttc ccg ggt ggc ggt cag atc gtt ggt | 18087 |
| Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly | |
| 1790 1795 1800 | |
| gga gtt tac ttg ttg ccg cgc agg ggc cct aga ttg ggt gtg cgc gcg | 18135 |
| Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala | |
| 1805 1810 1815 | |
| acg aga aag act tcc gag cgg tcg caa cct cga ggt aga cgt cag cct | 18183 |
| Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro | |
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| atc ccc aag gct cgt cgg ccc gag ggc agg acc tgg gct cag ccc ggg | 18231 |
| Ile Pro Lys Ala Arg Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly | |
| 1840 1845 1850 | |
| tac cct tgg ccc ctc tat ggc aat gag ggc tgc ggg tgg gcg gga tgg | 18279 |
| Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp | |
| 1855 1860 1865 | |
| ctc ctg tct ccc cgt ggc tct cgg cct agc tgg ggc ccc aca gac ccc | 18327 |
| Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro | |
| 1870 1875 1880 | |
| cgg cgt agg tcg cgc aat ttg ggt aag gtc atc gat acc ctt acg tgc | 18375 |
| Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys | |
| 1885 1890 1895 | |
| ggc ttc gcc gac ctc atg ggg tac ata ccg ctc gtc ggc gcc cct ctt | 18423 |
| Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Leu | |
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 1935 1940

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<223> Description of Artificial Sequence:

pd.delta.NS3NS5.pj.core173

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 35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
 50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
 65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
 85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
 100 105 110

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
 115 120 125

Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
 130 135 140

Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
 145 150 155 160

Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala
 165 170 175

Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val
 180 185 190

Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe
 195 200 205

Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe

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Met Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val
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Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr
      15              20              25

atg tcc aag gct cat ggg atc gat cct aac atc agg acc ggg gtg aga 12807
Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg
      30              35              40

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Thr Ile Thr Thr Gly Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe
      45              50              55

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| Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys | |
| 60 65 70 75 | |
| gac gag tgc cac tcc acg gat gcc aca tcc atc ttg ggc att ggc act | 12951 |
| Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr | |
| 80 85 90 | |
| gtc ctt gac caa gca gag act gcg ggg gcg aga ctg gtt gtg ctc gcc | 12999 |
| Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala | |
| 95 100 105 | |
| acc gcc acc cct ccg ggc tcc gtc act gtg ccc cat ccc aac atc gag | 13047 |
| Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile Glu | |
| 110 115 120 | |
| gag gtt gct ctg tcc acc acc gga gag atc cct ttt tac ggc aag gct | 13095 |
| Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala | |
| 125 130 135 | |
| atc ccc ctc gaa gta atc aag ggg ggg aga cat ctc atc ttc tgt cat | 13143 |
| Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe Cys His | |
| 140 145 150 155 | |
| tca aag aag aag tgc gac gaa ctc gcc gca aag ctg gtc gca ttg ggc | 13191 |
| Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly | |
| 160 165 170 | |
| atc aat gcc gtg gcc tac tac cgc ggt ctt gac gtg tcc gtc atc ccg | 13239 |
| Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro | |
| 175 180 185 | |
| acc agc ggc gat gtt gtc gtc gtg gca acc gat gcc ctc atg acc ggc | 13287 |
| Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr Gly | |
| 190 195 200 | |
| tat acc ggc gac ttc gac tcg gtg ata gac tgc aat acg tgt gtc acc | 13335 |
| Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr | |
| 205 210 215 | |
| cag aca gtc gat ttc agc ctt gac cct acc ttc acc att gag aca atc | 13383 |
| Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile | |
| 220 225 230 235 | |
| acg ctc ccc caa gat gct gtc tcc cgc act caa cgt cgg ggc agg act | 13431 |
| Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr | |
| 240 245 250 | |
| ggc agg ggg aag cca ggc atc tac aga ttt gtg gca ccg ggg gag cgc | 13479 |
| Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg | |
| 255 260 265 | |
| ccc tcc ggc atg ttc gac tcg tcc gtc ctc tgt gag tgc tat gac gca | 13527 |
| Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala | |
| 270 275 280 | |
| ggc tgt gct tgg tat gag ctc acg ccc gcc gag act aca gtt agg cta | 13575 |
| Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu | |
| 285 290 295 | |

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| cga gcg tac atg aac acc ccg ggg ctt ccc gtg tgc cag gac cat ctt | 13623 |
| Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu | |
| 300 305 310 315 | |
| gaa ttt tgg gag ggc gtc ttt aca ggc ctc act cat ata gat gcc cac | 13671 |
| Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp Ala His | |
| 320 325 330 | |
| ttt cta tcc cag aca aag cag agt ggg gag aac ctt cct tac ctg gta | 13719 |
| Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val | |
| 335 340 345 | |
| gcg tac caa gcc acc gtg tgc gct agg gct caa gcc cct ccc cca tcg | 13767 |
| Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser | |
| 350 355 360 | |
| tgg gac cag atg tgg aag tgt ttg att cgc ctc aag ccc acc ctc cat | 13815 |
| Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His | |
| 365 370 375 | |
| ggg cca aca ccc ctg cta tac aga ctg ggc gct gtt cag aat gaa atc | 13863 |
| Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile | |
| 380 385 390 395 | |
| acc ctg acg cac cca gtc acc aaa tac atc atg aca tgc atg tcg gcc | 13911 |
| Thr Leu Thr His Pro Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala | |
| 400 405 410 | |
| gac ctg gag gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc gtc ctg | 13959 |
| Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu | |
| 415 420 425 | |
| gct gct ttg gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc ata gtg | 14007 |
| Ala Ala Leu Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val | |
| 430 435 440 | |
| ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa | 14055 |
| Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu | |
| 445 450 455 | |
| gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag cac tta | 14103 |
| Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu | |
| 460 465 470 475 | |
| ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag | 14151 |
| Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys | |
| 480 485 490 | |
| gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc | 14199 |
| Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala | |
| 495 500 505 | |
| cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag | 14247 |
| Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys | |
| 510 515 520 | |
| cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca | 14295 |
| His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser | |
| 525 530 535 | |

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|---|-------|
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| Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala | |
| 540 545 550 555 | |
| gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc aac ata | 14391 |
| Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile | |
| 560 565 570 | |
| ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act | 14439 |
| Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr | |
| 575 580 585 | |
| gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga | 14487 |
| Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly | |
| 590 595 600 | |
| ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg | 14535 |
| Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val | |
| 605 610 615 | |
| gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc | 14583 |
| Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser | |
| 620 625 630 635 | |
| acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc | 14631 |
| Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala | |
| 640 645 650 | |
| ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc | 14679 |
| Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly | |
| 655 660 665 | |
| ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc | 14727 |
| Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala | |
| 670 675 680 | |
| tcc egg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat | 14775 |
| Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp | |
| 685 690 695 | |
| gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta acc cag | 14823 |
| Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln | |
| 700 705 710 715 | |
| ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc act cca | 14871 |
| Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro | |
| 720 725 730 | |
| tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg | 14919 |
| Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val | |
| 735 740 745 | |
| ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg | 14967 |
| Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu | |
| 750 755 760 | |
| cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg | 15015 |
| Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp | |
| 765 770 775 | |

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|---|-------|
| cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct gag atc | 15063 |
| Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile | |
| 780 785 790 795 | |
| act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc | 15111 |
| Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr | |
| 800 805 810 | |
| tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg | 15159 |
| Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr | |
| 815 820 825 | |
| ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg | 15207 |
| Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp | |
| 830 835 840 | |
| agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc | 15255 |
| Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe | |
| 845 850 855 | |
| cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag | 15303 |
| His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln | |
| 860 865 870 875 | |
| gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat | 15351 |
| Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His | |
| 880 885 890 | |
| agg ttt gcg ccc ccc tgc aag ccc ttg ctg cgg gag gag gta tca ttc | 15399 |
| Arg Phe Ala Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe | |
| 895 900 905 | |
| aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag | 15447 |
| Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu | |
| 910 915 920 | |
| ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc | 15495 |
| Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser | |
| 925 930 935 | |
| cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc | 15543 |
| His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro | |
| 940 945 950 955 | |
| ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca tct ctc | 15591 |
| Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu | |
| 960 965 970 | |
| aag gca act tgc acc gct aac cat gac tcc cct gat gct gag ctc ata | 15639 |
| Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile | |
| 975 980 985 | |
| gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg | 15687 |
| Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg | |
| 990 995 1000 | |
| gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt | 15735 |
| Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu | |
| 1005 1010 1015 | |

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|---|-------|
| gtg gcg gag gag gac gag cgg gag atc tcc gta ccc gca gaa atc ctg | 15783 |
| Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu | |
| 1020 1025 1030 1035 | |
| cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg cgg ccg | 15831 |
| Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro | |
| 1040 1045 1050 | |
| gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa | 15879 |
| Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu | |
| 1055 1060 1065 | |
| cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct | 15927 |
| Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro | |
| 1070 1075 1080 | |
| gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa tca acc | 15975 |
| Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr | |
| 1085 1090 1095 | |
| cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc | 16023 |
| Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser | |
| 1100 1105 1110 1115 | |
| tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct gag ccc | 16071 |
| Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro | |
| 1120 1125 1130 | |
| gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc | 16119 |
| Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser | |
| 1135 1140 1145 | |
| atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg | 16167 |
| Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly | |
| 1150 1155 1160 | |
| tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc | 16215 |
| Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys | |
| 1165 1170 1175 | |
| tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg tgc gcc | 16263 |
| Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala | |
| 1180 1185 1190 1195 | |
| gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta | 16311 |
| Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu | |
| 1200 1205 1210 | |
| cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct tgc caa | 16359 |
| Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln | |
| 1215 1220 1225 | |
| agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat | 16407 |
| Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His | |
| 1230 1235 1240 | |
| tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag | 16455 |
| Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys | |
| 1245 1250 1255 | |

| | | | | | | | | | | | | | | | | |
|---|--|--|--|-----------------|--|--|--|---------------------|--|--|--|-----------------|--|--|--|-------|
| gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac | | | | | | | | | | | | | | | | 16503 |
| Ala Asn Leu Leu | | | | Ser Val Glu Glu | | | | Ala Cys Ser Leu Thr | | | | Pro Pro His | | | | |
| 1260 | | | | 1265 | | | | 1270 | | | | 1275 | | | | |
| tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat | | | | | | | | | | | | | | | | 16551 |
| Ser Ala Lys Ser | | | | Lys Phe Gly Tyr | | | | Gly Ala Lys Asp | | | | Val Arg Cys His | | | | |
| | | | | 1280 | | | | 1285 | | | | 1290 | | | | |
| gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg | | | | | | | | | | | | | | | | 16599 |
| Ala Arg Lys Ala | | | | Val Thr His Ile | | | | Asn Ser Val Trp | | | | Lys Asp Leu Leu | | | | |
| 1295 | | | | 1300 | | | | 1305 | | | | | | | | |
| gaa gac aat gta aca cca ata gac act acc atc atg gct aag aac gag | | | | | | | | | | | | | | | | 16647 |
| Glu Asp Asn Val | | | | Thr Pro Ile Asp | | | | Thr Thr Ile Met | | | | Ala Lys Asn Glu | | | | |
| 1310 | | | | 1315 | | | | 1320 | | | | | | | | |
| gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc | | | | | | | | | | | | | | | | 16695 |
| Val Phe Cys Val | | | | Gln Pro Glu Lys | | | | Gly Gly Arg Lys | | | | Pro Ala Arg Leu | | | | |
| 1325 | | | | 1330 | | | | 1335 | | | | | | | | |
| atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg | | | | | | | | | | | | | | | | 16743 |
| Ile Val Phe Pro | | | | Asp Leu Gly Val | | | | Arg Val Cys Glu | | | | Lys Met Ala Leu | | | | |
| 1340 | | | | 1345 | | | | 1350 | | | | 1355 | | | | |
| tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac | | | | | | | | | | | | | | | | 16791 |
| Tyr Asp Val Val | | | | Thr Lys Leu Pro | | | | Leu Ala Val Met | | | | Gly Ser Ser Tyr | | | | |
| 1360 | | | | 1365 | | | | 1370 | | | | | | | | |
| gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg | | | | | | | | | | | | | | | | 16839 |
| Gly Phe Gln Tyr | | | | Ser Pro Gly Gln | | | | Arg Val Glu Phe | | | | Leu Val Gln Ala | | | | |
| 1375 | | | | 1380 | | | | 1385 | | | | | | | | |
| tgg aag tcc aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc | | | | | | | | | | | | | | | | 16887 |
| Trp Lys Ser Lys | | | | Lys Thr Pro Met | | | | Gly Phe Ser Tyr | | | | Asp Thr Arg Cys | | | | |
| 1390 | | | | 1395 | | | | 1400 | | | | | | | | |
| ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag gca atc | | | | | | | | | | | | | | | | 16935 |
| Phe Asp Ser Thr | | | | Val Thr Glu Ser | | | | Asp Ile Arg Thr | | | | Glu Glu Ala Ile | | | | |
| 1405 | | | | 1410 | | | | 1415 | | | | | | | | |
| tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc | | | | | | | | | | | | | | | | 16983 |
| Tyr Gln Cys Cys | | | | Asp Leu Asp Pro | | | | Gln Ala Arg Val | | | | Ala Ile Lys Ser | | | | |
| 1420 | | | | 1425 | | | | 1430 | | | | 1435 | | | | |
| ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg | | | | | | | | | | | | | | | | 17031 |
| Leu Thr Glu Arg | | | | Leu Tyr Val Gly | | | | Gly Pro Leu Thr | | | | Asn Ser Arg Gly | | | | |
| 1440 | | | | 1445 | | | | 1450 | | | | | | | | |
| gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act | | | | | | | | | | | | | | | | 17079 |
| Glu Asn Cys Gly | | | | Tyr Arg Arg Cys | | | | Arg Ala Ser Gly | | | | Val Leu Thr Thr | | | | |
| 1455 | | | | 1460 | | | | 1465 | | | | | | | | |
| agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt | | | | | | | | | | | | | | | | 17127 |
| Ser Cys Gly Asn | | | | Thr Leu Thr Cys | | | | Tyr Ile Lys Ala | | | | Arg Ala Ala Cys | | | | |
| 1470 | | | | 1475 | | | | 1480 | | | | | | | | |
| cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac | | | | | | | | | | | | | | | | 17175 |
| Arg Ala Ala Gly | | | | Leu Gln Asp Cys | | | | Thr Met Leu Val | | | | Cys Gly Asp Asp | | | | |
| 1485 | | | | 1490 | | | | 1495 | | | | | | | | |

| | |
|---|-------|
| tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc | 17223 |
| Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser | |
| 1500 1505 1510 1515 | |
| ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg | 17271 |
| Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly | |
| 1520 1525 1530 | |
| gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc | 17319 |
| Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser | |
| 1535 1540 1545 | |
| tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac | 17367 |
| Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr | |
| 1550 1555 1560 | |
| ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca | 17415 |
| Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr | |
| 1565 1570 1575 | |
| gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc atg ttt | 17463 |
| Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe | |
| 1580 1585 1590 1595 | |
| gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc ttt agc | 17511 |
| Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser | |
| 1600 1605 1610 | |
| gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc gag atc | 17559 |
| Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile | |
| 1615 1620 1625 | |
| tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca atc att | 17607 |
| Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile | |
| 1630 1635 1640 | |
| caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac tct cca | 17655 |
| Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro | |
| 1645 1650 1655 | |
| ggg gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg gta ccg | 17703 |
| Gly Glu Ile Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro | |
| 1660 1665 1670 1675 | |
| ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct agg ctt | 17751 |
| Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu | |
| 1680 1685 1690 | |
| ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc ttc aac | 17799 |
| Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn | |
| 1695 1700 1705 | |
| tgg gca gta aga aca aag ctc aaa ctc act cca ata gcg gcc gct ggc | 17847 |
| Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly | |
| 1710 1715 1720 | |
| cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg gga gac | 17895 |
| Gln Leu Asp Leu Ser Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp | |
| 1725 1730 1735 | |

att tat cac agc gtg tct cat gcc cgg ccc cgc tgg atc tgg ttt tgc 17943
 Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys
 1740 1745 1750 1755

cta ctc ctg ctt gct gca ggg gta ggc atc tac ctc ctc ccc aac cga 17991
 Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
 1760 1765 1770

atg agc acg aat cct aaa cct caa aga aag acc aaa cgt aac acc aac 18039
 Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn
 1775 1780 1785

cgg cgg ccg cag gac gtc aag ttc ccg ggt ggc ggt cag atc gtt ggt 18087
 Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
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gga gtt tac ttg ttg ccg cgc agg ggc cct aga ttg ggt gtg cgc gcg 18135
 Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala
 1805 1810 1815

acg aga aag act tcc gag cgg tcg caa cct cga ggt aga cgt cag cct 18183
 Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
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atc ccc aag gct cgt cgg ccc gag ggc agg acc tgg gct cag ccc ggg 18231
 Ile Pro Lys Ala Arg Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly
 1840 1845 1850

tac cct tgg ccc ctc tat ggc aat gag ggc tgc ggg tgg gcg gga tgg 18279
 Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp
 1855 1860 1865

ctc ctg tct ccc cgt ggc tct cgg cct agc tgg ggc ccc aca gac ccc 18327
 Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro
 1870 1875 1880

cgg cgt agg tcg cgc aat ttg ggt aag gtc atc gat acc ctt acg tgc 18375
 Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys
 1885 1890 1895

ggc ttc gcc gac ctc atg ggg tac ata ccg ctc gtc taatagtcga 18421
 Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val
 1900 1905 1910

ctttgttccc actgtacttt tagctcgtac aaaatacaat atacttttca tttctccgta 18481
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<211> 1911

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:

pd.delta.NS3NS5.pj.core140

<400> 17

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| 1 | | | | | 5 | | | | 10 | | | | | 15 | |

Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His
 20 25 30
 Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
 35 40 45
 Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
 50 55 60
 Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
 65 70 75 80
 Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
 85 90 95
 Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
 100 105 110
 Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
 115 120 125
 Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
 130 135 140
 Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys
 145 150 155 160
 Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly Ile Asn Ala Val Ala
 165 170 175
 Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ser Gly Asp Val
 180 185 190
 Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe
 195 200 205
 Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe
 210 215 220
 Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile Thr Leu Pro Gln Asp
 225 230 235 240
 Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr Gly Arg Gly Lys Pro
 245 250 255
 Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg Pro Ser Gly Met Phe
 260 265 270
 Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr
 275 280 285
 Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu Arg Ala Tyr Met Asn
 290 295 300
 Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Gly
 305 310 315 320
 Val Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr
 325 330 335

Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val Ala Tyr Gln Ala Thr
 340 345 350
 Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp
 355 360 365
 Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu
 370 375 380
 Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile Thr Leu Thr His Pro
 385 390 395 400
 Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala Asp Leu Glu Val Val
 405 410 415
 Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala
 420 425 430
 Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val Gly Arg Val Val Leu
 435 440 445
 Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Arg Glu
 450 455 460
 Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln
 465 470 475 480
 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
 485 490 495
 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
 500 505 510
 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
 515 520 525
 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn
 530 535 540
 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
 545 550 555 560
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 565 570 575
 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
 580 585 590
 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
 610 615 620
 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
 625 630 635 640
 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655

Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
 675 680 685
 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu
 705 710 715 720
 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735
 Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
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 Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile
 770 775 780
 Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
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 Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
 805 810 815
 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
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 Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser Ala Glu
 835 840 845
 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
 850 855 860
 Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln Val Pro Ser Pro Glu
 865 870 875 880
 Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro
 885 890 895
 Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
 900 905 910
 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
 Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu
 930 935 940
 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
 Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr
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Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
 980 985 990
 Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn
 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
 1010 1015 1020
 Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Arg Arg
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 Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro Asp Tyr Asn Pro Pro
 1045 1050 1055
 Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val Val His
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 Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Pro Arg
 1075 1080 1085
 Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr Leu Ser Thr Ala Leu
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 Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser Ser Thr Ser Gly Ile
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 Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro Ala Pro Ser Gly Cys
 1125 1130 1135
 Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu
 1140 1145 1150
 Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val
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 1170 1175 1180
 Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys
 185 1190 1195 1200
 Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu
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 Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys Lys Val
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 Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu
 1235 1240 1245
 Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys Ala Asn Leu Leu Ser
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 Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys
 265 1270 1275 1280
 Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys Ala Val
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Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu Glu Asp Asn Val Thr
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 Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln
 1315 1320 1325
 Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp
 1330 1335 1340
 Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Thr
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 Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys
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 Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val
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 Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr
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 Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr
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 Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys
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 Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro
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 Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val
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 Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro
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 Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro
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 Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp
 585 1590 1595 1600
 Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg
 1605 1610 1615

Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr
 1620 1625 1630
 Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly
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 Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Ala Trp
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 Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ala Arg Gly Gly
 1685 1690 1695
 Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Arg Thr
 1700 1705 1710
 Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly Gln Leu Asp Leu Ser
 1715 1720 1725
 Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Val
 1730 1735 1740
 Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys Leu Leu Leu Leu Ala
 745 1750 1755 1760
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 gac gag tgc cac tcc acg gat gcc aca tcc atc ttg ggc att ggc act 12951
 Asp Glu Cys His Ser Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr
 80 85 90
 gtc ctt gac caa gca gag act gcg ggg gcg aga ctg gtt gtg ctc gcc 12999
 Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala
 95 100 105
 acc gcc acc cct ccg ggc tcc gtc act gtg ccc cat ccc aac atc gag 13047
 Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn Ile Glu
 110 115 120
 gag gtt gct ctg tcc acc acc gga gag atc cct ttt tac ggc aag gct 13095
 Glu Val Ala Leu Ser Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala
 125 130 135
 atc ccc ctc gaa gta atc aag ggg ggg aga cat ctc atc ttc tgt cat 13143
 Ile Pro Leu Glu Val Ile Lys Gly Gly Arg His Leu Ile Phe Cys His
 140 145 150 155
 tca aag aag aag tgc gac gaa ctc gcc gca aag ctg gtc gca ttg ggc 13191
 Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Val Ala Leu Gly
 160 165 170

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|---|-------|
| atc aat gcc gtg gcc tac tac cgc ggt ctt gac gtg tcc gtc atc ccg Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro 175 180 185 | 13239 |
| acc agc ggc gat gtt gtc gtc gtg gca acc gat gcc ctc atg acc ggc Thr Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr Gly 190 195 200 | 13287 |
| tat acc ggc gac ttc gac tcg gtg ata gac tgc aat acg tgt gtc acc Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr 205 210 215 | 13335 |
| cag aca gtc gat ttc agc ctt gac cct acc ttc acc att gag aca atc Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Ile 220 225 230 235 | 13383 |
| acg ctc ccc caa gat gct gtc tcc cgc act caa cgt cgg ggc agg act Thr Leu Pro Gln Asp Ala Val Ser Arg Thr Gln Arg Arg Gly Arg Thr 240 245 250 | 13431 |
| ggc agg ggg aag cca ggc atc tac aga ttt gtg gca ccg ggg gag cgc Gly Arg Gly Lys Pro Gly Ile Tyr Arg Phe Val Ala Pro Gly Glu Arg 255 260 265 | 13479 |
| ccc tcc ggc atg ttc gac tcg tcc gtc ctc tgt gag tgc tat gac gca Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala 270 275 280 | 13527 |
| ggc tgt gct tgg tat gag ctc acg ccc gcc gag act aca gtt agg cta Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu 285 290 295 | 13575 |
| cga gcg tac atg aac acc ccg ggg ctt ccc gtg tgc cag gac cat ctt Arg Ala Tyr Met Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu 300 305 310 315 | 13623 |
| gaa ttt tgg gag ggc gtc ttt aca ggc ctc act cat ata gat gcc cac Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr His Ile Asp Ala His 320 325 330 | 13671 |
| ttt cta tcc cag aca aag cag agt ggg gag aac ctt cct tac ctg gta Phe Leu Ser Gln Thr Lys Gln Ser Gly Glu Asn Leu Pro Tyr Leu Val 335 340 345 | 13719 |
| gcg tac caa gcc acc gtg tgc gct agg gct caa gcc cct ccc cca tcg Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser 350 355 360 | 13767 |
| tgg gac cag atg tgg aag tgt ttg att cgc ctc aag ccc acc ctc cat Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His 365 370 375 | 13815 |
| ggg cca aca ccc ctg cta tac aga ctg ggc gct gtt cag aat gaa atc Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile 380 385 390 395 | 13863 |
| acc ctg acg cac cca gtc acc aaa tac atc atg aca tgc atg tcg gcc Thr Leu Thr His Pro Val Thr Lys Tyr Ile Met Thr Cys Met Ser Ala 400 405 410 | 13911 |

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|---|-------|
| gac ctg gag gtc gtc acg agc acc tgg gtg ctc gtt ggc ggc gtc ctg | 13959 |
| Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly Val Leu | |
| 415 420 425 | |
| gct gct ttg gcc gcg tat tgc ctg tca aca ggc tgc gtg gtc ata gtg | 14007 |
| Ala Ala Leu Ala Ala Tyr Cys Leu Ser Thr Gly Cys Val Val Ile Val | |
| 430 435 440 | |
| ggc agg gtc gtc ttg tcc ggg aag ccg gca atc ata cct gac agg gaa | 14055 |
| Gly Arg Val Val Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu | |
| 445 450 455 | |
| gtc ctc tac cga gag ttc gat gag atg gaa gag tgc tct cag cac tta | 14103 |
| Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu | |
| 460 465 470 475 | |
| ccg tac atc gag caa ggg atg atg ctc gcc gag cag ttc aag cag aag | 14151 |
| Pro Tyr Ile Glu Gln Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys | |
| 480 485 490 | |
| gcc ctc ggc ctc ctg cag acc gcg tcc cgt cag gca gag gtt atc gcc | 14199 |
| Ala Leu Gly Leu Leu Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala | |
| 495 500 505 | |
| cct gct gtc cag acc aac tgg caa aaa ctc gag acc ttc tgg gcg aag | 14247 |
| Pro Ala Val Gln Thr Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys | |
| 510 515 520 | |
| cat atg tgg aac ttc atc agt ggg ata caa tac ttg gcg ggc ttg tca | 14295 |
| His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser | |
| 525 530 535 | |
| acg ctg cct ggt aac ccc gcc att gct tca ttg atg gct ttt aca gct | 14343 |
| Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala | |
| 540 545 550 555 | |
| gct gtc acc agc cca cta acc act agc caa acc ctc ctc ttc aac ata | 14391 |
| Ala Val Thr Ser Pro Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile | |
| 560 565 570 | |
| ttg ggg ggg tgg gtg gct gcc cag ctc gcc gcc ccc ggt gcc gct act | 14439 |
| Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr | |
| 575 580 585 | |
| gcc ttt gtg ggc gct ggc tta gct ggc gcc gcc atc ggc agt gtt gga | 14487 |
| Ala Phe Val Gly Ala Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly | |
| 590 595 600 | |
| ctg ggg aag gtc ctc ata gac atc ctt gca ggg tat ggc gcg ggc gtg | 14535 |
| Leu Gly Lys Val Leu Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val | |
| 605 610 615 | |
| gcg gga gct ctt gtg gca ttc aag atc atg agc ggt gag gtc ccc tcc | 14583 |
| Ala Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser | |
| 620 625 630 635 | |
| acg gag gac ctg gtc aat cta ctg ccc gcc atc ctc tcg ccc gga gcc | 14631 |
| Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala | |
| 640 645 650 | |

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|---|-------|
| ctc gta gtc ggc gtg gtc tgt gca gca ata ctg cgc cgg cac gtt ggc | 14679 |
| Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His Val Gly | |
| 655 660 665 | |
| ccg ggc gag ggg gca gtg cag tgg atg aac cgg ctg ata gcc ttc gcc | 14727 |
| Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala | |
| 670 675 680 | |
| tcc cgg ggg aac cat gtt tcc ccc acg cac tac gtg ccg gag agc gat | 14775 |
| Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp | |
| 685 690 695 | |
| gca gct gcc cgc gtc act gcc ata ctc agc agc ctc act gta acc cag | 14823 |
| Ala Ala Ala Arg Val Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln | |
| 700 705 710 715 | |
| ctc ctg agg cga ctg cac cag tgg ata agc tcg gag tgt acc act cca | 14871 |
| Leu Leu Arg Arg Leu His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro | |
| 720 725 730 | |
| tgc tcc ggt tcc tgg cta agg gac atc tgg gac tgg ata tgc gag gtg | 14919 |
| Cys Ser Gly Ser Trp Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val | |
| 735 740 745 | |
| ttg agc gac ttt aag acc tgg cta aaa gct aag ctc atg cca cag ctg | 14967 |
| Leu Ser Asp Phe Lys Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu | |
| 750 755 760 | |
| cct ggg atc ccc ttt gtg tcc tgc cag cgc ggg tat aag ggg gtc tgg | 15015 |
| Pro Gly Ile Pro Phe Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp | |
| 765 770 775 | |
| cga ggg gac ggc atc atg cac act cgc tgc cac tgt gga gct gag atc | 15063 |
| Arg Gly Asp Gly Ile Met His Thr Arg Cys His Cys Gly Ala Glu Ile | |
| 780 785 790 795 | |
| act gga cat gtc aaa aac ggg acg atg agg atc gtc ggt cct agg acc | 15111 |
| Thr Gly His Val Lys Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr | |
| 800 805 810 | |
| tgc agg aac atg tgg agt ggg acc ttc ccc att aat gcc tac acc acg | 15159 |
| Cys Arg Asn Met Trp Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr | |
| 815 820 825 | |
| ggc ccc tgt acc ccc ctt cct gcg ccg aac tac acg ttc gcg cta tgg | 15207 |
| Gly Pro Cys Thr Pro Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp | |
| 830 835 840 | |
| agg gtg tct gca gag gaa tac gtg gag ata agg cag gtg ggg gac ttc | 15255 |
| Arg Val Ser Ala Glu Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe | |
| 845 850 855 | |
| cac tac gtg acg ggt atg act act gac aat ctt aaa tgc ccg tgc cag | 15303 |
| His Tyr Val Thr Gly Met Thr Thr Asp Asn Leu Lys Cys Pro Cys Gln | |
| 860 865 870 875 | |
| gtc cca tcg ccc gaa ttt ttc aca gaa ttg gac ggg gtg cgc cta cat | 15351 |
| Val Pro Ser Pro Glu Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His | |
| 880 885 890 | |

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|---|-------|
| agg ttt gcg ccc ccc tgc aag ccc ttg ctg cgg gag gag gta tca ttc | 15399 |
| Arg Phe Ala Pro Pro Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe | |
| 895 900 905 | |
| aga gta gga ctc cac gaa tac ccg gta ggg tcg caa tta cct tgc gag | 15447 |
| Arg Val Gly Leu His Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu | |
| 910 915 920 | |
| ccc gaa ccg gac gtg gcc gtg ttg acg tcc atg ctc act gat ccc tcc | 15495 |
| Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser | |
| 925 930 935 | |
| cat ata aca gca gag gcg gcc ggg cga agg ttg gcg agg gga tca ccc | 15543 |
| His Ile Thr Ala Glu Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro | |
| 940 945 950 955 | |
| ccc tct gtg gcc agc tcc tcg gct agc cag cta tcc gct cca tct ctc | 15591 |
| Pro Ser Val Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu | |
| 960 965 970 | |
| aag gca act tgc acc gct aac cat gac tcc cct gat gct gag ctc ata | 15639 |
| Lys Ala Thr Cys Thr Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile | |
| 975 980 985 | |
| gag gcc aac ctc cta tgg agg cag gag atg ggc ggc aac atc acc agg | 15687 |
| Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg | |
| 990 995 1000 | |
| gtt gag tca gaa aac aaa gtg gtg att ctg gac tcc ttc gat ccg ctt | 15735 |
| Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu | |
| 1005 1010 1015 | |
| gtg gcg gag gag gac gag cgg gag atc tcc gta ccc gca gaa atc ctg | 15783 |
| Val Ala Glu Glu Asp Glu Arg Glu Ile Ser Val Pro Ala Glu Ile Leu | |
| 1020 1025 1030 1035 | |
| cgg aag tct cgg aga ttc gcc cag gcc ctg ccc gtt tgg gcg cgg ccg | 15831 |
| Arg Lys Ser Arg Arg Phe Ala Gln Ala Leu Pro Val Trp Ala Arg Pro | |
| 1040 1045 1050 | |
| gac tat aac ccc ccg cta gtg gag acg tgg aaa aag ccc gac tac gaa | 15879 |
| Asp Tyr Asn Pro Pro Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu | |
| 1055 1060 1065 | |
| cca cct gtg gtc cat ggc tgc ccg ctt cca cct cca aag tcc cct cct | 15927 |
| Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro | |
| 1070 1075 1080 | |
| gtg cct ccg cct cgg aag aag cgg acg gtg gtc ctc act gaa tca acc | 15975 |
| Val Pro Pro Pro Arg Lys Lys Arg Thr Val Val Leu Thr Glu Ser Thr | |
| 1085 1090 1095 | |
| cta tct act gcc ttg gcc gag ctc gcc acc aga agc ttt ggc agc tcc | 16023 |
| Leu Ser Thr Ala Leu Ala Glu Leu Ala Thr Arg Ser Phe Gly Ser Ser | |
| 1100 1105 1110 1115 | |
| tca act tcc ggc att acg ggc gac aat acg aca aca tcc tct gag ccc | 16071 |
| Ser Thr Ser Gly Ile Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro | |
| 1120 1125 1130 | |

gcc cct tct ggc tgc ccc ccc gac tcc gac gct gag tcc tat tcc tcc 16119
 Ala Pro Ser Gly Cys Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser
 1135 1140 1145

atg ccc ccc ctg gag ggg gag cct ggg gat ccg gat ctt agc gac ggg 16167
 Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly
 1150 1155 1160

tca tgg tca acg gtc agt agt gag gcc aac gcg gag gat gtc gtg tgc 16215
 Ser Trp Ser Thr Val Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys
 1165 1170 1175

tgc tca atg tct tac tct tgg aca ggc gca ctc gtc acc ccg tgc gcc 16263
 Cys Ser Met Ser Tyr Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala
 1180 1185 1190 1195

gcg gaa gaa cag aaa ctg ccc atc aat gca cta agc aac tcg ttg cta 16311
 Ala Glu Glu Gln Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu
 1200 1205 1210

cgt cac cac aat ttg gtg tat tcc acc acc tca cgc agt gct tgc caa 16359
 Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln
 1215 1220 1225

agg cag aag aaa gtc aca ttt gac aga ctg caa gtt ctg gac agc cat 16407
 Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His
 1230 1235 1240

tac cag gac gta ctc aag gag gtt aaa gca gcg gcg tca aaa gtg aag 16455
 Tyr Gln Asp Val Leu Lys Glu Val Lys Ala Ala Ala Ser Lys Val Lys
 1245 1250 1255

gct aac ttg cta tcc gta gag gaa gct tgc agc ctg acg ccc cca cac 16503
 Ala Asn Leu Leu Ser Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His
 1260 1265 1270 1275

tca gcc aaa tcc aag ttt ggt tat ggg gca aaa gac gtc cgt tgc cat 16551
 Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His
 1280 1285 1290

gcc aga aag gcc gta acc cac atc aac tcc gtg tgg aaa gac ctt ctg 16599
 Ala Arg Lys Ala Val Thr His Ile Asn Ser Val Trp Lys Asp Leu Leu
 1295 1300 1305

gaa gac aat gta aca cca ata gac act acc atc atg gct aag aac gag 16647
 Glu Asp Asn Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu
 1310 1315 1320

gtt ttc tgc gtt cag cct gag aag ggg ggt cgt aag cca gct cgt ctc 16695
 Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu
 1325 1330 1335

atc gtg ttc ccc gat ctg ggc gtg cgc gtg tgc gaa aag atg gct ttg 16743
 Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu
 1340 1345 1350 1355

tac gac gtg gtt aca aag ctc ccc ttg gcc gtg atg gga agc tcc tac 16791
 Tyr Asp Val Val Thr Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr
 1360 1365 1370

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|---|-------|
| gga ttc caa tac tca cca gga cag cgg gtt gaa ttc ctc gtg caa gcg | 16839 |
| Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala | |
| 1375 1380 1385 | |
| tgg aag tcc aag aaa acc cca atg ggg ttc tcg tat gat acc cgc tgc | 16887 |
| Trp Lys Ser Lys Lys Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys | |
| 1390 1395 1400 | |
| ttt gac tcc aca gtc act gag agc gac atc cgt acg gag gag gca atc | 16935 |
| Phe Asp Ser Thr Val Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile | |
| 1405 1410 1415 | |
| tac caa tgt tgt gac ctc gac ccc caa gcc cgc gtg gcc atc aag tcc | 16983 |
| Tyr Gln Cys Cys Asp Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser | |
| 1420 1425 1430 1435 | |
| ctc acc gag agg ctt tat gtt ggg ggc cct ctt acc aat tca agg ggg | 17031 |
| Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly | |
| 1440 1445 1450 | |
| gag aac tgc ggc tat cgc agg tgc cgc gcg agc ggc gta ctg aca act | 17079 |
| Glu Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr | |
| 1455 1460 1465 | |
| agc tgt ggt aac acc ctc act tgc tac atc aag gcc cgg gca gcc tgt | 17127 |
| Ser Cys Gly Asn Thr Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys | |
| 1470 1475 1480 | |
| cga gcc gca ggg ctc cag gac tgc acc atg ctc gtg tgt ggc gac gac | 17175 |
| Arg Ala Ala Gly Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp | |
| 1485 1490 1495 | |
| tta gtc gtt atc tgt gaa agc gcg ggg gtc cag gag gac gcg gcg agc | 17223 |
| Leu Val Val Ile Cys Glu Ser Ala Gly Val Gln Glu Asp Ala Ala Ser | |
| 1500 1505 1510 1515 | |
| ctg aga gcc ttc acg gag gct atg acc agg tac tcc gcc ccc cct ggg | 17271 |
| Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly | |
| 1520 1525 1530 | |
| gac ccc cca caa cca gaa tac gac ttg gag ctc ata aca tca tgc tcc | 17319 |
| Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser | |
| 1535 1540 1545 | |
| tcc aac gtg tca gtc gcc cac gac ggc gct gga aag agg gtc tac tac | 17367 |
| Ser Asn Val Ser Val Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr | |
| 1550 1555 1560 | |
| ctc acc cgt gac cct aca acc ccc ctc gcg aga gct gcg tgg gag aca | 17415 |
| Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr | |
| 1565 1570 1575 | |
| gca aga cac act cca gtc aat tcc tgg cta ggc aac ata atc atg ttt | 17463 |
| Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe | |
| 1580 1585 1590 1595 | |
| gcc ccc aca ctg tgg gcg agg atg ata ctg atg acc cat ttc ttt agc | 17511 |
| Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser | |
| 1600 1605 1610 | |

gtc ctt ata gcc agg gac cag ctt gaa cag gcc ctc gat tgc gag atc 17559
 Val Leu Ile Ala Arg Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile
 1615 1620 1625

tac ggg gcc tgc tac tcc ata gaa cca ctg gat cta cct cca atc att 17607
 Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile
 1630 1635 1640

caa aga ctc cat ggc ctc agc gca ttt tca ctc cac agt tac tct cca 17655
 Gln Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro
 1645 1650 1655

ggt gaa atc aat agg gtg gcc gca tgc ctc aga aaa ctt ggg gta ccg 17703
 Gly Glu Ile Asn Arg Val Ala Ala Cys Leu Arg Lys Leu Gly Val Pro
 1660 1665 1670 1675

ccc ttg cga gct tgg aga cac cgg gcc cgg agc gtc cgc gct agg ctt 17751
 Pro Leu Arg Ala Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu
 1680 1685 1690

ctg gcc aga gga ggc agg gct gcc ata tgt ggc aag tac ctc ttc aac 17799
 Leu Ala Arg Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr Leu Phe Asn
 1695 1700 1705

tgg gca gta aga aca aag ctc aaa ctc act cca ata gcg gcc gct ggc 17847
 Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Ala Ala Ala Gly
 1710 1715 1720

cag ctg gac ttg tcc ggc tgg ttc acg gct ggc tac agc ggg gga gac 17895
 Gln Leu Asp Leu Ser Gly Trp Phe Thr Ala Gly Tyr Ser Gly Gly Asp
 1725 1730 1735

att tat cac agc gtg tct cat gcc cgg ccc cgc tgg atc tgg ttt tgc 17943
 Ile Tyr His Ser Val Ser His Ala Arg Pro Arg Trp Ile Trp Phe Cys
 1740 1745 1750 1755

cta ctc ctg ctt gct gca ggg gta ggc atc tac ctc ctc ccc aac cga 17991
 Leu Leu Leu Leu Ala Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
 1760 1765 1770

atg agc acg aat cct aaa cct caa aga aag acc aaa cgt aac acc aac 18039
 Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn
 1775 1780 1785

cgg cgg ccg cag gac gtc aag ttc ccg ggt ggc ggt cag atc gtt ggt 18087
 Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
 1790 1795 1800

gga gtt tac ttg ttg ccg cgc agg ggc cct aga ttg ggt gtg cgc gcg 18135
 Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala
 1805 1810 1815

acg aga aag act tcc gag cgg tcg caa cct cga ggt aga cgt cag cct 18183
 Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
 1820 1825 1830 1835

atc ccc aag gct cgt cgg ccc gag ggc agg acc tgg gct cag ccc ggg 18231
 Ile Pro Lys Ala Arg Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly
 1840 1845 1850

tac cct tgg ccc ctc tat ggc aat gag ggc tgc ggg tgg gcg gga tgg 18279
 Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp
 1855 1860 1865

ctc ctg tct ccc cgt ggc tct cgg cct agc tgg ggc ccc aca gac ccc 18327
 Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro
 1870 1875 1880

cgg cgt agg tgc cgc aat ttg ggt aag gtc atc gat acc ctt acg tgc 18375
 Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys
 1885 1890 1895

ggc ttc gcc gac ctc atg ggg tac ata ccg ctc gtc ggc gcc cct ctt 18423
 Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Leu
 1900 1905 1910 1915

gga ggc gct gcc agg gcc taatagtcga ctttgttccc actgtacttt 18471
 Gly Gly Ala Ala Arg Ala
 1920

tagctcgtac aaaataacaat atactttttca tttctccgta aacaacatgt tttcccatgt 18531
 aatataccttt tctatttttcc gttccggttac caactttaca catactttat atagctattc 18591
 acttctatac actaaaaaac taagacaatt ttaattttgc tgccctgccat atttcaattt 18651
 gttataaatt cctataaatt atcctattag tagctaaaaa aagatgaatg tgaatcgaat 18711
 cctaagagaa ttggatctga tccacaggac ggggtgtggc gccatgatcg cgtagtcgat 18771
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<213> Artificial Sequence

<220>

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pd.delta.NS3NS5.pj.core150

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Gly Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly
 35 40 45

Ser Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly
 50 55 60

Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser
 65 70 75 80

Thr Asp Ala Thr Ser Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala
 85 90 95

Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro
 100 105 110

Gly Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser
 115 120 125

Thr Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Leu Glu Val
 130 135 140

Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 145 | | 150 | | 155 | | 160 | | | | | | | | | |
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| | | | | 165 | | | | | 170 | | | | | 175 | |
| Tyr | Tyr | Arg | Gly | Leu | Asp | Val | Ser | Val | Ile | Pro | Thr | Ser | Gly | Asp | Val |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Val | Val | Val | Ala | Thr | Asp | Ala | Leu | Met | Thr | Gly | Tyr | Thr | Gly | Asp | Phe |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Asp | Ser | Val | Ile | Asp | Cys | Asn | Thr | Cys | Val | Thr | Gln | Thr | Val | Asp | Phe |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Ser | Leu | Asp | Pro | Thr | Phe | Thr | Ile | Glu | Thr | Ile | Thr | Leu | Pro | Gln | Asp |
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| Ala | Val | Ser | Arg | Thr | Gln | Arg | Arg | Gly | Arg | Thr | Gly | Arg | Gly | Lys | Pro |
| | | | | 245 | | | | 250 | | | | | | 255 | |
| Gly | Ile | Tyr | Arg | Phe | Val | Ala | Pro | Gly | Glu | Arg | Pro | Ser | Gly | Met | Phe |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Asp | Ser | Ser | Val | Leu | Cys | Glu | Cys | Tyr | Asp | Ala | Gly | Cys | Ala | Trp | Tyr |
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| Glu | Leu | Thr | Pro | Ala | Glu | Thr | Thr | Val | Arg | Leu | Arg | Ala | Tyr | Met | Asn |
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| Thr | Pro | Gly | Leu | Pro | Val | Cys | Gln | Asp | His | Leu | Glu | Phe | Trp | Glu | Gly |
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| Val | Phe | Thr | Gly | Leu | Thr | His | Ile | Asp | Ala | His | Phe | Leu | Ser | Gln | Thr |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Lys | Gln | Ser | Gly | Glu | Asn | Leu | Pro | Tyr | Leu | Val | Ala | Tyr | Gln | Ala | Thr |
| | | | 340 | | | | 345 | | | | | | 350 | | |
| Val | Cys | Ala | Arg | Ala | Gln | Ala | Pro | Pro | Pro | Ser | Trp | Asp | Gln | Met | Trp |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Lys | Cys | Leu | Ile | Arg | Leu | Lys | Pro | Thr | Leu | His | Gly | Pro | Thr | Pro | Leu |
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| Leu | Tyr | Arg | Leu | Gly | Ala | Val | Gln | Asn | Glu | Ile | Thr | Leu | Thr | His | Pro |
| 385 | | | | | 390 | | | | | 395 | | | | 400 | |
| Val | Thr | Lys | Tyr | Ile | Met | Thr | Cys | Met | Ser | Ala | Asp | Leu | Glu | Val | Val |
| | | | | 405 | | | | | 410 | | | | | 415 | |
| Thr | Ser | Thr | Trp | Val | Leu | Val | Gly | Gly | Val | Leu | Ala | Ala | Leu | Ala | Ala |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Tyr | Cys | Leu | Ser | Thr | Gly | Cys | Val | Val | Ile | Val | Gly | Arg | Val | Val | Leu |
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| Ser | Gly | Lys | Pro | Ala | Ile | Ile | Pro | Asp | Arg | Glu | Val | Leu | Tyr | Arg | Glu |
| | 450 | | | | | 455 | | | | | 460 | | | | |

Phe Asp Glu Met Glu Glu Cys Ser Gln His Leu Pro Tyr Ile Glu Gln
 465 470 475 480
 Gly Met Met Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu
 485 490 495
 Gln Thr Ala Ser Arg Gln Ala Glu Val Ile Ala Pro Ala Val Gln Thr
 500 505 510
 Asn Trp Gln Lys Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe
 515 520 525
 Ile Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn
 530 535 540
 Pro Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ala Val Thr Ser Pro
 545 550 555 560
 Leu Thr Thr Ser Gln Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val
 565 570 575
 Ala Ala Gln Leu Ala Ala Pro Gly Ala Ala Thr Ala Phe Val Gly Ala
 580 585 590
 Gly Leu Ala Gly Ala Ala Ile Gly Ser Val Gly Leu Gly Lys Val Leu
 595 600 605
 Ile Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val
 610 615 620
 Ala Phe Lys Ile Met Ser Gly Glu Val Pro Ser Thr Glu Asp Leu Val
 625 630 635 640
 Asn Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val
 645 650 655
 Val Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala
 660 665 670
 Val Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His
 675 680 685
 Val Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val
 690 695 700
 Thr Ala Ile Leu Ser Ser Leu Thr Val Thr Gln Leu Leu Arg Arg Leu
 705 710 715 720
 His Gln Trp Ile Ser Ser Glu Cys Thr Thr Pro Cys Ser Gly Ser Trp
 725 730 735
 Leu Arg Asp Ile Trp Asp Trp Ile Cys Glu Val Leu Ser Asp Phe Lys
 740 745 750
 Thr Trp Leu Lys Ala Lys Leu Met Pro Gln Leu Pro Gly Ile Pro Phe
 755 760 765
 Val Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile
 770 775 780

Met His Thr Arg Cys His Cys Gly Ala Glu Ile Thr Gly His Val Lys
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 Asn Gly Thr Met Arg Ile Val Gly Pro Arg Thr Cys Arg Asn Met Trp
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 Ser Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro
 820 825 830
 Leu Pro Ala Pro Asn Tyr Thr Phe Ala Leu Trp Arg Val Ser Ala Glu
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 Glu Tyr Val Glu Ile Arg Gln Val Gly Asp Phe His Tyr Val Thr Gly
 850 855 860
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 Phe Phe Thr Glu Leu Asp Gly Val Arg Leu His Arg Phe Ala Pro Pro
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 Cys Lys Pro Leu Leu Arg Glu Glu Val Ser Phe Arg Val Gly Leu His
 900 905 910
 Glu Tyr Pro Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val
 915 920 925
 Ala Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu
 930 935 940
 Ala Ala Gly Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Val Ala Ser
 945 950 955 960
 Ser Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr
 965 970 975
 Ala Asn His Asp Ser Pro Asp Ala Glu Leu Ile Glu Ala Asn Leu Leu
 980 985 990
 Trp Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn
 995 1000 1005
 Lys Val Val Ile Leu Asp Ser Phe Asp Pro Leu Val Ala Glu Glu Asp
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 Leu Val Glu Thr Trp Lys Lys Pro Asp Tyr Glu Pro Pro Val Val His
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 Gly Cys Pro Leu Pro Pro Pro Lys Ser Pro Pro Val Pro Pro Pro Arg
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 1090 1095 1100

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 Thr Gly Asp Asn Thr Thr Thr Ser Ser Glu Pro Ala Pro Ser Gly Cys
 1125 1130 1135
 Pro Pro Asp Ser Asp Ala Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu
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 Gly Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val
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 Ser Ser Glu Ala Asn Ala Glu Asp Val Val Cys Cys Ser Met Ser Tyr
 1170 1175 1180
 Ser Trp Thr Gly Ala Leu Val Thr Pro Cys Ala Ala Glu Glu Gln Lys
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 Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Leu
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 Val Tyr Ser Thr Thr Ser Arg Ser Ala Cys Gln Arg Gln Lys Lys Val
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 Thr Phe Asp Arg Leu Gln Val Leu Asp Ser His Tyr Gln Asp Val Leu
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 1250 1255 1260
 Val Glu Glu Ala Cys Ser Leu Thr Pro Pro His Ser Ala Lys Ser Lys
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 Phe Gly Tyr Gly Ala Lys Asp Val Arg Cys His Ala Arg Lys Ala Val
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 Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp
 1330 1335 1340
 Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Thr
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 Lys Leu Pro Leu Ala Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser
 1365 1370 1375
 Pro Gly Gln Arg Val Glu Phe Leu Val Gln Ala Trp Lys Ser Lys Lys
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 Thr Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val
 1395 1400 1405
 Thr Glu Ser Asp Ile Arg Thr Glu Glu Ala Ile Tyr Gln Cys Cys Asp
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Leu Asp Pro Gln Ala Arg Val Ala Ile Lys Ser Leu Thr Glu Arg Leu
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 Tyr Val Gly Gly Pro Leu Thr Asn Ser Arg Gly Glu Asn Cys Gly Tyr
 1445 1450 1455
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 Leu Thr Cys Tyr Ile Lys Ala Arg Ala Ala Cys Arg Ala Ala Gly Leu
 1475 1480 1485
 Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val Val Ile Cys
 1490 1495 1500
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 Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val
 1540 1545 1550
 Ala His Asp Gly Ala Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro
 1555 1560 1565
 Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro
 1570 1575 1580
 Val Asn Ser Trp Leu Gly Asn Ile Ile Met Phe Ala Pro Thr Leu Trp
 585 1590 1595 1600
 Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Val Leu Ile Ala Arg
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 Asp Gln Leu Glu Gln Ala Leu Asp Cys Glu Ile Tyr Gly Ala Cys Tyr
 1620 1625 1630
 Ser Ile Glu Pro Leu Asp Leu Pro Pro Ile Ile Gln Arg Leu His Gly
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 1730 1735 1740

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 Ala Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg Met Ser Thr Asn Pro
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 Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn Arg Arg Pro Gln Asp
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 1795 1800 1805
 Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala Thr Arg Lys Thr Ser
 1810 1815 1820
 Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro Ile Pro Lys Ala Arg
 825 1830 1835 1840
 Arg Pro Glu Gly Arg Thr Trp Ala Gln Pro Gly Tyr Pro Trp Pro Leu
 1845 1850 1855
 Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp Leu Leu Ser Pro Arg
 1860 1865 1870
 Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro Arg Arg Arg Ser Arg
 1875 1880 1885
 Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys Gly Phe Ala Asp Leu
 1890 1895 1900
 Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Leu Gly Gly Ala Ala Arg
 905 1910 1915 1920
 Ala

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